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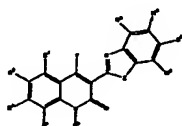
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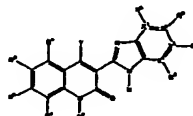
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(54) Title: QUINOLINONE DERIVATIVES



(I)



(II)

(57) Abstract: Organic compounds having the formulas (I) and (II) are provided where the variables have the values described herein. Medicaments include an anti-cancer drug selected from 5-FU or CPT 11 and a compound of formula (I) or formula (II), a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer in treatin along with an anti-cancer drug selected from 5-FU or CPT-11. The medicaments may be used in treating cancer. The use of a compound of formula (I) or formula (II), a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer in treating cancer in conjunction with an anti-cancer drug selected from 5-FU or CPT-11 is also provided.

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## QUINOLINONE DERIVATIVES

### FIELD OF THE INVENTION

This invention pertains generally to treating diseases characterized by angiogenesis including cancer. More specifically, the invention described herein  
5 pertains to treating diseases characterized by activity of vascular endothelial growth factor receptor tyrosine kinases. The present invention provides, small molecule inhibitors of vascular endothelial growth factor receptor tyrosine kinase, pharmaceutical formulations containing such inhibitors, methods of treating patients with such pharmaceutical formulations, and to methods of preparing such  
10 pharmaceutical formulations and inhibitors.

### BACKGROUND OF THE INVENTION

Capillaries reach into almost all tissues of the human body and supply tissues with oxygen and nutrients as well as removing waste products. Under typical conditions, the endothelial cells lining the capillaries do not divide, and  
15 capillaries, therefore, do not normally increase in number or size in a human adult. Under certain normal conditions, however, such as when a tissue is damaged, or during certain parts of the menstrual cycle, the capillaries begin to proliferate rapidly. This process of forming new capillaries from pre-existing blood vessels is known as angiogenesis or neovascularization. See Folkman, J. Scientific American  
20 275, 150-154 (1996). Angiogenesis during wound healing is an example of pathophysiological neovascularization during adult life. During wound healing, the additional capillaries provide a supply of oxygen and nutrients, promote granulation tissue, and aid in waste removal. After termination of the healing process, the capillaries normally regress. Lymboussaki, A. "Vascular Endothelial Growth  
25 Factors and their Receptors in Embryos, Adults, and in Tumors" Academic Dissertation, University of Helsinki, Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute, (1999).

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Angiogenesis also plays an important role in the growth of cancer cells. It is known that once a nest of cancer cells reaches a certain size, roughly 1 to 2 mm in diameter, the cancer cells must develop a blood supply in order for the tumor to grow larger as diffusion will not be sufficient to supply the cancer cells with enough oxygen and nutrients. Thus, inhibition of angiogenesis is expected to halt the growth of cancer cells.

Receptor tyrosine kinases (RTKs) are transmembrane polypeptides that regulate developmental cell growth and differentiation, remodeling and regeneration of adult tissues. Mustonen, T. et al., *J. Cell Biology* 129, 895-898 (1995); van der Geer, P. et al. *Ann Rev. Cell Biol.* 10, 251-337 (1994). Polypeptide ligands known as growth factors or cytokines, are known to activate RTKs. Signaling RTKs involves ligand binding and a shift in conformation in the external domain of the receptor resulting in its dimerization. Lymboussaki, A. "Vascular Endothelial Growth Factors and their Receptors in Embryos, Adults, and in Tumors" Academic Dissertation, University of Helsinki, Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute, (1999); Ullrich, A. et al., *Cell* 61, 203-212 (1990). Binding of the ligand to the RTK results in receptor trans-phosphorylation at specific tyrosine residues and subsequent activation of the catalytic domains for the phosphorylation of cytoplasmic substrates. Id.

Two subfamilies of RTKs are specific to the vascular endothelium. These include the vascular endothelial growth factor (VEGF) subfamily and the Tie receptor subfamily. Class III RTKs include VEGFR-1, VEGFR-2, and VEGFR-3. Shibuya, M. et al., *Oncogene* 5, 519-525 (1990); Terman, B. et al., *Oncogene* 6, 1677-1683 (1991); Aprelikova, O. et al., *Cancer Res.* 52, 746-748 (1992).

Members of the VEGF subfamily have been described as being able to induce vascular permeability and endothelial cell proliferation and further identified as a major inducer of angiogenesis and vasculogenesis. Ferrara, N. et al., *Endocrinol. Rev.* 18, 4-25 (1997). VEGF is known to specifically bind to RTKs

including VEGFR-1 and VEGFR-2. DeVries, C. et al., Science 255, 989-991 (1992); Quinn, T. et al., Proc. Natl. Acad. Sci. 90, 7533-7537 (1993). VEGF stimulates the migration and proliferation of endothelial cells and induces angiogenesis both *in vitro* and *in vivo*. Connolly, D. et al., J. Biol. Chem. 264, 20017-20024 (1989); Connolly, D. et al., J. Clin. Invest. 84, 1470-1478 (1989); Ferrara, N. et al., Endocrino. Rew. 18, 4-25 (1997); Leung, D. et al., Science 246, 1306-1309 (1989); Plouet, J. et al., EMBO J 8, 3801-3806 (1989).

Because angiogenesis is known to be critical to the growth of cancer and to be controlled by VEGF and VEGF-RTK, substantial efforts have been undertaken to develop therapeutics that are antagonists of VEGF-RTK to thereby inhibit or retard angiogenesis, and, hopefully, interfere or stop tumor proliferation.

A wide variety of chemical compounds and compositions have been reported as having activity against one of more the VEGF-RTKs. Examples include quinoline derivatives such as described in WO 98/13350, aminonicotinamide derivatives (see, *e.g.*, WO 01/55114), antisense compounds (see, *e.g.*, WO 01/52904), peptidomimetics (see, *e.g.*, WO 01/52875), quinazoline derivatives (see, *e.g.*, U.S. Patent No. 6,258,951) monoclonal antibodies (see, *e.g.*, EP 1 086 705 A1), various 5,10,15,20-tetraaryl-porphyrins and 5,10,15-triaryl-corroles (see, *e.g.*, WO 00/27379), heterocyclic alkanesulfonic and alkane carboxylic acid derivatives (see, *e.g.*, DE19841985), oxindolylquinazoline derivatives (see, *e.g.*, WO 99/10349), 1,4-diazaanthracene derivatives (see, *e.g.*, U.S. Patent No. 5,763,441), and cinnoline derivatives (see, *e.g.*, WO 97/34876), and various indazole compounds (see, *e.g.*, WO 01/02369 and WO 01/53268).

Various indolyl substituted compounds have recently been disclosed in WO 01/29025, WO 01/62251, and WO 01/62252, and various benzimidazolyl compounds have recently been disclosed in WO 01/28993. These compounds are reportedly capable of inhibiting, modulating, and/or regulating signal transduction of both receptor-type and non-receptor tyrosine kinases. Some of the disclosed



compounds contain a quinolone fragment bonded to the indolyl or benzimidazolyl group.

The synthesis of 4-hydroxy quinolone and 4-hydroxy quinoline derivatives is disclosed in a number of references. For example, Ukrainets et al. have disclosed the synthesis of 3-(benzimidazol-2-yl)-4-hydroxy-2-oxo-1,2-dihydroquinoline. Ukrainets, I. et al., Tet. Lett. 42, 7747-7748 (1995); Ukrainets, I. et al., Khimiya Geterotsiklicheskikh Soedinii, 2, 239-241(1992). Ukrainets has also disclosed the synthesis, anticonvulsive and antithyroid activity of other 4-hydroxy quinolones and thio analogs such as 1H-2-oxo-3-(2-benzimidazolyl)-4-hydroxyquinoline. Ukrainets, I. et al., Khimiya Geterotsiklicheskikh Soedinii, 1, 105-108 (1993); Ukrainets, I. et al., Khimiya Geterotsiklicheskikh Soedinii, 8, 1105-1108 (1993); Ukrainets, I. et al., Chem. Heterocyclic Comp. 33, 600-604, (1997).

The synthesis of various quinoline derivatives is disclosed in WO 97/48694. These compounds are disclosed as capable of binding to nuclear hormone receptors and being useful for stimulating osteoblast proliferation and bone growth. The compounds are also disclosed as being useful in the treatment or prevention of diseases associated with nuclear hormone receptor families.

Various quinoline derivatives in which the benzene ring of the quinolone is substituted with a sulfur group are disclosed in WO 92/18483. These compounds are disclosed as being useful in pharmaceutical formulations and as medicaments.

Quinolone and coumarin derivatives have been disclosed as having use in a variety of applications unrelated to medicine and pharmaceutical formulations. References that describe the preparation of quinolone derivatives for use in photopolymerizable compositions or for luminescent properties include: U.S. Patent No. 5,801,212 issued to Okamoto et al.; JP 8-29973; JP 7-43896; JP 6-9952; JP 63-258903; EP 797376; and DE 23 63 459.

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Despite the exploration of a variety of chemistries to provide VEGF-RTK-antagonist therapies, a continuing need exists for compounds that inhibit the proliferation of capillaries, inhibit the growth of tumors, and/or inhibit vascular endothelial growth factor receptor tyrosine kinase and pharmaceutical formulations that contain such compounds. A need also exists for methods for administering such compounds and pharmaceutical formulations to patients in need thereof.

### SUMMARY OF THE INVENTION

The present invention provides compounds, pharmaceutical formulations including the compounds, methods of preparing the pharmaceutical formulations, and methods of treating patients with the pharmaceutical formulations and compounds.

The invention provides a method of treating cancer, comprising administering to a patient a compound of formula I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer along with an anti-cancer drug selected from 5-FU (5-fluorouracil) or CPT-11 (irinotecan). The compound of formula I may be selected from one of four groups or embodiments of the groups.

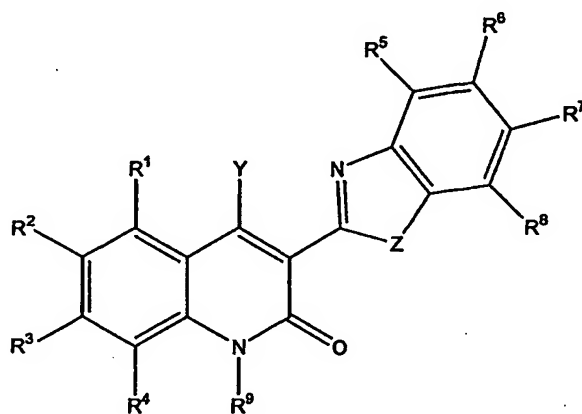
The invention also provides the use of a compound of formula I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer in treating cancer in conjunction with an anti-cancer drug selected from 5-FU or CPT-11. The compound of formula I may be selected from one of four groups or embodiments of the groups.

The invention also provides medicaments that include a compound of formula I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer in treating cancer and an anti-cancer drug selected from 5-FU or CPT-11. The invention further

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provides for the use of such medicaments. The compound of formula I may be selected from any of four groups or embodiments of the groups.

- The present invention provides a first group of compounds having the structure I. The invention also provides tautomers of the compounds,  
 5 pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers. Structure I has the following formula:



I

where, in the first group of compounds:

- Y is selected from -OR<sup>10</sup> groups, -C(=O)-R<sup>11</sup> groups, -NR<sup>12</sup>R<sup>13</sup>  
 10 groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or  
 15 unsubstituted heterocyclaminoalkyl groups, substituted or unsubstituted saturated heterocycl groups, substituted or unsubstituted heterocycloxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, or substituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or NR<sup>14</sup> groups;

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R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, or -C(=O)R<sup>18</sup> groups;

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> may be the same or different and are independently selected from H, Cl, Br, F, I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups, -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)R<sup>25</sup> groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted

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(heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

- R<sup>9</sup> and R<sup>14</sup> may be the same or different and are independently
- 5 selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups,
- 10 substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

- R<sup>10</sup> is selected from substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>,
- 15 -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups, -NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl), -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub>
- 20 groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, or substituted or unsubstituted heterocyclylalkyl groups;

- R<sup>11</sup> is selected from H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups,
- 25 -N(aryl)(heterocyclyl) groups, -O-alkyl groups, O-aryl groups, heterocyclyloxyalkyl groups, or substituted or unsubstituted aryl groups;

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R<sup>12</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

- R<sup>13</sup> is selected from substituted or unsubstituted alkyl groups,
- 5 substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups,
- 10 substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups,
- 15 -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted
- 20 or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted heterocycliloxyalkyl groups, or -C(=O)-N(alkyl)(heterocyclyl) groups;

- R<sup>15</sup> and R<sup>19</sup> may be the same or different and are independently
- 25 selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl)

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groups, -NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R<sup>16</sup> and R<sup>20</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R<sup>17</sup> and R<sup>21</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted

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heterocyclylaminoalkyl groups, substituted or unsubstituted  
diheterocyclylaminoalkyl groups, substituted or unsubstituted  
(heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted  
(heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl  
5 groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted  
aryloxyalkyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups, or  
-C(=O)-N(alkyl)(heterocyclyl) groups;

R<sup>18</sup>, R<sup>23</sup>, R<sup>24</sup>, and R<sup>25</sup> may be the same or different and are  
independently selected from H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups,  
10 -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl)  
groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,  
-N(heterocyclyl)<sub>2</sub> groups, substituted or unsubstituted alkyl groups, substituted or  
unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups,  
substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryloxy  
15 groups, heterocyclyloxy groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups,  
-N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, or  
-N(aryl)O-aryl groups; and

R<sup>22</sup> is selected from substituted or unsubstituted alkyl groups,  
substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl  
20 groups.

The invention provides a second group of compounds including  
compounds having the structure I, tautomers of the compounds, pharmaceutically  
acceptable salts of the compounds, and pharmaceutically acceptable salts of the  
tautomers.

25 In the second group of compounds:

Y is selected from -OR<sup>10</sup> groups, -C(=O)-R<sup>11</sup> groups, -NR<sup>12</sup>R<sup>13</sup>  
groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted  
heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups,



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substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted saturated  
5 heterocyclyl groups, substituted or unsubstituted heterocycloxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, or substituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or  $\text{NR}^{14}$  groups;

$\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , and  $\text{R}^4$  may be the same or different and are  
10 independently selected from H, Cl, Br, F, I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, and tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted  
15 or unsubstituted heterocyclyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted  
20 heterocyclylalkyl groups, or -C(=O)R<sup>18</sup> groups;

$\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ , and  $\text{R}^8$  may be the same or different and are  
independently selected from H, Cl, Br, F, I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups, -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted  
25 or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, and tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)R<sup>25</sup> groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted

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alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclaloxyalkyl groups;

$R^9$  is selected from the group consisting of -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

$R^{10}$  is selected from substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, or substituted or unsubstituted heterocyclylalkyl groups;

$R^{11}$  is selected from H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, -O-alkyl groups, O-aryl groups, substituted or unsubstituted alkyl groups, or substituted or unsubstituted aryl groups;

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R<sup>12</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R<sup>13</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocyclyl) groups, -C(=O)-N(alkyl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyoxyalkyl groups;

R<sup>14</sup> is selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups,

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substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

- R<sup>15</sup> and R<sup>19</sup> may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

- R<sup>16</sup> and R<sup>20</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

- R<sup>17</sup> and R<sup>21</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted

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alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, 5 -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocyclyl) groups, -C(=O)-N(alkyl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted 10 heterocycliloxyalkyl groups;

R<sup>18</sup>, R<sup>23</sup>, R<sup>24</sup>, and R<sup>25</sup> may be the same or different and are independently selected from H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups, 15 -N(heterocyclyl)<sub>2</sub> groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryloxy groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, or -N(aryl)O-aryl groups; 20 and

R<sup>22</sup> is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

The invention provides a third group of compounds including 25 compounds having the structure I, tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers.

In the third group of compounds:

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Y is selected from -OH, SH, alkylthio groups, arylthio groups, -OR<sup>10</sup> groups, -C(=O)-R<sup>11</sup> groups, -NR<sup>12</sup>R<sup>13</sup> groups, -CN, substituted or unsubstituted alkyl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted heterocycl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocycloxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, or substituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or NR<sup>14</sup> groups;

R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocycl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclalkyl groups, or -C(=O)R<sup>18</sup> groups;

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> may be the same or different and are independently selected from H, Cl, Br, F, I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups, -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted

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or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups,  $-C(=O)R^{25}$  groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycliloxyalkyl groups;

$R^9$  and  $R^{14}$  may be the same or different and are independently selected from H,  $-OH$ , substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups,  $-NH_2$ , substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl groups, or  $-C(=O)$ -aryl groups;

$R^{10}$  is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl groups,  $-C(=O)$ -aryl groups,  $-C(=O)O$ -alkyl groups,  $-C(=O)O$ -aryl groups,  $-C(=O)NH_2$ ,  $-C(=O)NH$ (alkyl) groups,  $-C(=O)NH$ (aryl) groups,  $-C(=O)N$ (alkyl)<sub>2</sub> groups,  $-C(=O)N$ (aryl)<sub>2</sub> groups,  $-C(=O)N$ (alkyl)(aryl) groups,  $-NH_2$ ,  $-NH$ (alkyl) groups,  $-NH$ (aryl) groups,  $-N$ (alkyl)<sub>2</sub> groups,  $-N$ (alkyl)(aryl) groups,  $-N$ (aryl)<sub>2</sub> groups,  $-C(=O)NH$ (heterocyclyl) groups,

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-C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, or  
-C(=O)N(aryl)(heterocyclyl) groups;

R<sup>11</sup> is selected from H, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>,  
-NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups,  
5 -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, -NH(heterocyclyl)  
groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, or substituted or  
unsubstituted aryl groups;

R<sup>12</sup> is selected from H, substituted or unsubstituted alkyl groups,  
substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl  
10 groups;

R<sup>13</sup> is selected from H, substituted or unsubstituted alkyl groups,  
substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl  
groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted  
heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted  
15 or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted  
dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups,  
substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted  
(alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups,  
substituted or unsubstituted arylamino groups, substituted or unsubstituted  
20 dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or  
unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups,  
-C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>,  
-C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups,  
-C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl  
25 groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
-C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups,  
-C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted  
heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups,



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substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

R<sup>15</sup> and R<sup>19</sup> may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

R<sup>16</sup> and R<sup>20</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R<sup>17</sup> and R<sup>21</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted

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- alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups,
- 5 -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted
- 10 heterocycloxyalkyl groups;

- R<sup>18</sup>, R<sup>23</sup>, R<sup>24</sup>, and R<sup>25</sup> may be the same or different and are independently selected from H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,
- 15 -N(heterocyclyl)<sub>2</sub> groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyl groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, or -N(aryl)O-aryl groups;
- 20 and

R<sup>22</sup> is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

- In the third group of compounds, at least one of R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, or R<sup>8</sup> is
- 25 selected from substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted saturated heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or

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unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;  $-OR^{19}$  groups where  $R^{19}$  is selected from substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups,  $-C(=O)H$ ,  $-C(=O)$ -aryl groups,  $-C(=O)NH_2$ ,  $-C(=O)NH$ (alkyl) groups,  $-C(=O)NH$ (aryl) groups,  $-C(=O)N$ (alkyl)<sub>2</sub> groups,  $-C(=O)N$ (aryl)<sub>2</sub> groups,  $-C(=O)N$ (alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted and unsubstituted heterocyclyloxyalkyl groups;  $-NR^{20}R^{21}$  groups where  $R^{20}$  is selected from substituted or unsubstituted heterocyclyl groups;  $-NR^{20}R^{21}$  groups where  $R^{21}$  is selected from substituted or unsubstituted heterocyclyl groups,  $-C(=O)H$ ,  $-C(=O)$ -aryl groups,  $-C(=O)NH_2$ ,  $-C(=O)NH$ (alkyl) groups,  $-C(=O)NH$ (aryl) groups,  $-C(=O)N$ (alkyl)<sub>2</sub> groups,  $-C(=O)N$ (aryl)<sub>2</sub> groups,  $-C(=O)N$ (alkyl)(aryl) groups,  $-C(=O)O$ -alkyl groups,  $-C(=O)O$ -aryl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or

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unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups; or  $-C(=O)R^{25}$  groups where  $R^{25}$  is selected from H,  $-NH_2$ ,  $-NH(\text{alkyl})$  groups,  $-NH(\text{aryl})$  groups,  $-N(\text{alkyl})_2$  groups,  $-N(\text{aryl})_2$  groups,   
5  $-N(\text{alkyl})(\text{aryl})$  groups,  $-NH(\text{heterocyclyl})$  groups,  $-N(\text{heterocyclyl})(\text{alkyl})$  groups,  $-N(\text{heterocyclyl})(\text{aryl})$  groups,  $-N(\text{heterocyclyl})_2$  groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aryloxy groups, or substituted or unsubstituted heterocyclyl groups.

The invention provides a fourth group of compounds having the   
10 structure I, tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers.

In the fourth group of compounds:

Y is selected from  $-OH$ ,  $SH$ , alkylthio groups, arylthio groups,  $-OR^{10}$  groups,  $-C(=O)-R^{11}$  groups,  $-NR^{12}R^{13}$  groups,  $-CN$ , substituted or unsubstituted   
15 alkyl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted   
20 diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocycloxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, or substituted   
25 or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or  $NR^{14}$  groups;

$R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  may be the same or different and are independently selected from H, Cl, Br, F, I,  $-CN$ ,  $-NO_2$ ,  $-OH$ ,  $-OR^{15}$  groups,

-NR<sup>16</sup>R<sup>17</sup> groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, or -C(=O)R<sup>18</sup> groups;

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> may be the same or different and are independently selected from H, Cl, Br, F, I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups, -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)R<sup>25</sup> groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

R<sup>9</sup> and R<sup>14</sup> may be the same or different and are independently selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted alkylamino groups,

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substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or  
5 -C(=O)-aryl groups;

R<sup>10</sup> is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl  
10 groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, or  
15 -C(=O)N(aryl)(heterocyclyl) groups;

R<sup>11</sup> is selected from H, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, -NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, or substituted or  
20 unsubstituted aryl groups;

R<sup>12</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R<sup>13</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted  
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- dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted
- 5 dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl
- 10 groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted
- 15 aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

- R<sup>15</sup> and R<sup>19</sup> may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups,
- 20 -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted
- 25 diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups,

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substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

- R<sup>16</sup> and R<sup>20</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or  
 5 unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

- R<sup>17</sup> and R<sup>21</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups,  
 -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>,  
 10 -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups,  
 15 substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocyclyl) groups, -C(=O)-N(aryl)(heterocyclyl) groups,  
 20 substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

- R<sup>18</sup>, R<sup>23</sup>, R<sup>24</sup>, and R<sup>25</sup> may be the same or different and are  
 25 independently selected from H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups, -N(heterocyclyl)<sub>2</sub> groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups,



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substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyl groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, or -N(aryl)O-aryl groups; and

5                   R<sup>22</sup> is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

In the fourth group of compounds, at least one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, or R<sup>4</sup> is an -OR<sup>15</sup> group and R<sup>15</sup> is selected from substituted or unsubstituted  
10 heterocyclylalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclyl groups,  
15 substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, or substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups.

Preferred compounds in any of the first, second, or third groups  
20 described above are provided in which Z is an -NR<sup>14</sup>. Preferred compound of the fourth group are also provided in which Z is an -NR<sup>10</sup> group.

Preferred compounds according to the first, second, third, and fourth groups of compounds are provided in which Y is an -OR<sup>10</sup> group, an -NR<sup>12</sup>R<sup>13</sup> group, or a substituted or unsubstituted alkynyl group.

25                   Other preferred compounds of the first, second, third, and fourth groups are provided in which R<sup>1</sup> is selected from H, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or

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unsubstituted heterocycloxy groups, or substituted or unsubstituted heterocyclyl groups.

Still further provided are compounds of the first, second, third, and fourth groups in which  $R^2$  is selected from the group consisting of H, F, Cl,  $-NO_2$ ,  
5 substituted and unsubstituted heterocyclalkoxy groups, and substituted and unsubstituted heterocyclyl groups.

Still further provided are compounds of the first, second, third, and fourth groups in which  $R^6$  or  $R^7$  is an alkyl group. Still further preferred compounds of the four groups are those in which  $R^6$  or  $R^7$  is an  $-OR^{19}$  group and  $R^{19}$   
10 is an alkyl group, an aryl group, a heterocyclyl group, or a heterocyclalkyl group.

Preferred compounds of the fourth group of compounds are provided in which  $R^1$  is an  $-OR^{15}$  group and  $R^{15}$  is selected from substituted or unsubstituted heterocyclalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted  
15 aminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclaminoalkyl groups, substituted or unsubstituted diheterocyclaminoalkyl groups, substituted or unsubstituted  
20 (heterocyclyl)(alkyl)aminoalkyl groups, or substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups.

The invention also provides a method of treating cancer, comprising administering to a patient a compound of formula II, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable  
25 salt of the tautomer along with an anti-cancer drug selected from 5-FU or CPT-11.

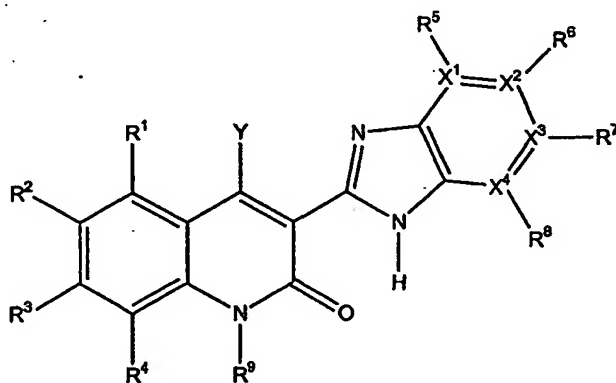
The invention also provides the use of a compound of formula II, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a

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pharmaceutically acceptable salt of the tautomer in treating cancer in conjunction with an anti-cancer drug selected from 5-FU or CPT-11.

The invention also provides medicaments that include a compound of formula II, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer in treating cancer and an anti-cancer drug selected from 5-FU or CPT-11. The invention further provides for the use of such medicaments.

The invention further provides compounds having the structure II. The invention provides tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers. Structure II has the following formula



II

where:

Y is selected from H, -OH, -OR<sup>10</sup> groups, -SH, -SR<sup>11</sup> groups, -NR<sup>12</sup>R<sup>13</sup> groups, -CN, -C(=O)-R<sup>14</sup> groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl

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groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclaminoalkyl groups, substituted or unsubstituted heterocycl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

$X^1$ ,  $X^2$ ,  $X^3$ , and  $X^4$  are selected from C or N, and at least one of  $X^1$ ,  $X^2$ ,  $X^3$ , and  $X^4$  is N;

$R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ , and  $R^8$  may be the same or different and are independently selected from H, Cl, Br, F, I,  $-NO_2$ ,  $-CN$ ,  $-OH$ ,  $-OR^{15}$  groups,  $-NR^{16}R^{17}$  groups,  $-C(=O)R^{18}$  groups,  $-SH$ ,  $-SR^{19}$  groups,  $-S(=O)R^{20}$  groups,  $S(=O)_2R^{21}$  groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocycl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;  $R^5$  is absent or is H if  $X^1$  is N;  $R^6$  is absent or is H if  $X^2$  is N;  $R^7$  is absent or is H if  $X^3$  is N; and  $R^8$  is absent or is H if  $X^4$  is N;

$R^9$  is selected from H,  $-OH$ , substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups,  $-NH_2$ , substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted

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diaryl amino groups, substituted or unsubstituted (alkyl)(aryl) amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R<sup>10</sup> is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, or -C(=O)N(aryl)(heterocyclyl) groups;

R<sup>11</sup> and R<sup>19</sup> may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, or substituted or unsubstituted aryl groups;

R<sup>12</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R<sup>13</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted

dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, 5 -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, 10 substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycliloxyalkyl groups;

R<sup>14</sup> is selected from H, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, substituted or 15 unsubstituted aryl groups, -NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, or -N(aryl)(heterocyclyl) groups;

R<sup>12</sup> and R<sup>13</sup> may join together to form a 5 to 7 membered saturated or unsaturated, substituted or unsubstituted N-containing ring;

R<sup>15</sup> is selected from substituted or unsubstituted alkyl groups, 20 substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl 25 groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted

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diheterocyclylaminoalkyl groups, substituted or unsubstituted  
 (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted  
 (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkoxyalkyl  
 groups, substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted  
 5 hydroxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

R<sup>16</sup> is selected from H, substituted or unsubstituted alkyl groups,  
 substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl  
 groups;

R<sup>17</sup> is selected from H, substituted or unsubstituted alkyl groups,  
 10 substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl  
 groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>,  
 -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups,  
 -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups,  
 -C(=O)O-aryl groups, substituted or unsubstituted aminoalkyl groups, substituted or  
 15 unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl  
 groups, substituted or unsubstituted arylaminoalkyl groups, substituted or  
 unsubstituted diarylaminoalkyl groups, substituted or unsubstituted  
 (aryl)(alkyl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl  
 groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups,  
 20 -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)<sub>2</sub> groups,  
 -C(=O)-N(alkyl)(heterocyclyl) groups, -C(=O)-N(aryl)(heterocyclyl) groups,  
 substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or  
 unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups,  
 substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted  
 25 heterocycloxyalkyl groups, -OH, substituted or unsubstituted alkoxy groups,  
 substituted or unsubstituted aryloxy groups, or -NH<sub>2</sub> groups;

R<sup>16</sup> and R<sup>17</sup> may join together to form a 5 to 7 membered saturated or  
 unsaturated, substituted or unsubstituted N-containing ring; and

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$R^{18}$ ,  $R^{20}$ , and  $R^{21}$  may be the same or different and are independently selected from H,  $-NH_2$ ,  $-NH(\text{alkyl})$  groups,  $-NH(\text{aryl})$  groups,  $-N(\text{alkyl})_2$  groups,  $-N(\text{aryl})_2$  groups,  $-N(\text{alkyl})(\text{aryl})$  groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups,  $-OH$ , substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyl groups,  $-NHOH$ ,  $-N(\text{alkyl})OH$  groups,  $-N(\text{aryl})OH$  groups,  $-N(\text{alkyl})O$ -alkyl groups,  $-N(\text{aryl})O$ -alkyl groups,  $-N(\text{alkyl})O$ -aryl groups, or  $-N(\text{aryl})O$ -aryl groups.

Preferred compounds having structure II are also provided where Y is selected from H,  $-OH$ ,  $-OR^{10}$  groups, or  $-NR^{12}R^{13}$  groups.

Still other preferred compounds having structure II are provided where at least two of  $X^1$ ,  $X^2$ ,  $X^3$ , and  $X^4$  are C and the corresponding substituents  $R^5$ ,  $R^6$ ,  $R^7$ , and  $R^8$  are hydrogen, and at least one of  $X^1$ ,  $X^2$ ,  $X^3$ , and  $X^4$  is N, and the rest of the compound is consistent with any of the above-described compounds.

Still other more preferred compounds of structure II are provided in which  $R^6$  or  $R^7$  is an alkyl group and the rest of the compound is consistent with any of the above-described compounds.

Still other compounds of structure II are provided in which  $R^6$  or  $R^7$  is an  $-OR^{15}$  group and  $R^{15}$  is an alkyl, aryl, heterocyclyl, or heterocyclylalkyl group and the rest of the molecule is consistent with any of the above-described compounds.

Still further compounds having the formula of structure II are provided in which  $R^1$  is selected from H, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclylalkoxy groups, substituted or unsubstituted heterocycloxy groups, or substituted or unsubstituted heterocyclyl groups.

Still other compounds having the Structure II are provided in which In other compounds having the structure II,  $R^2$  is selected from H, F, Cl,  $-NO_2$ ,



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substituted or unsubstituted heterocyclyl groups, or substituted or unsubstituted heterocyclylalkoxy groups.

Pharmaceutical formulations according to the present invention are provided which include any of the compounds described above in combination with  
5 a pharmaceutically acceptable carrier.

A method of treating a patient in need of an inhibitor of vascular endothelial growth factor receptor tyrosine kinase is provided which includes administering an effective amount of the pharmaceutical formulation according to the present invention to a patient in need thereof.

10 Further objects, features and advantages of the invention will be apparent from the following detailed description.

#### DETAILED DESCRIPTION OF THE INVENTION

The present invention provides novel compounds that act as antagonists of receptor tyrosine kinases, and, more particularly, as inhibitors of  
15 bFGF and/or VEGF-RTK function. The compounds provided herein can be formulated into pharmaceutical formulations that are useful in treating patients with a need for an inhibitor of VEGF-RTK, especially, in particular embodiments, to provide compositions and methods for reducing capillary proliferation and in the treatment of cancer.

20 The following abbreviations and definitions are used throughout this application:

“VEGF” is an abbreviation that stands for vascular endothelial growth factor.

“RTK” is an abbreviation that stands for receptor tyrosine kinase.

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"VEGF-RTK" is an abbreviation that stands for vascular endothelial growth factor receptor tyrosine kinase.

"Flt-1" is an abbreviation that stands for fms-like tyrosine kinase-1, also known as vascular endothelial growth factor receptor-1 or "VEGFR1".

5 "KDR" is an abbreviation that stands for kinase- insert domain-containing receptor, also known as vascular endothelial growth factor receptor-2 or "VEGFR2".

"bFGF" is an abbreviation that stands for basic fibroblast growth factor.

10 "bFGFR" is an abbreviation that stands for basic fibroblast growth factor receptor.

Generally, reference to a certain element such as hydrogen or H is meant to include all isotopes of that element. For example, if an R group is defined to include hydrogen or H, it also includes deuterium and tritium.

15 The phrase "unsubstituted alkyl" refers to alkyl groups that do not contain heteroatoms. Thus the phrase includes straight chain alkyl groups such as methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl, dodecyl and the like. The phrase also includes branched chain isomers of straight chain alkyl groups, including but not limited to, the following which are provided

20 by way of example:  $-\text{CH}(\text{CH}_3)_2$ ,  $-\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$ ,  $-\text{CH}(\text{CH}_2\text{CH}_3)_2$ ,  $-\text{C}(\text{CH}_3)_3$ ,  $-\text{C}(\text{CH}_2\text{CH}_3)_3$ ,  $-\text{CH}_2\text{CH}(\text{CH}_3)_2$ ,  $-\text{CH}_2\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$ ,  $-\text{CH}_2\text{CH}(\text{CH}_2\text{CH}_3)_2$ ,  $-\text{CH}_2\text{C}(\text{CH}_3)_3$ ,  $-\text{CH}_2\text{C}(\text{CH}_2\text{CH}_3)_3$ ,  $-\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$ ,  $-\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)_2$ ,  $-\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$ ,  $-\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_2\text{CH}_3)_2$ ,  $-\text{CH}_2\text{CH}_2\text{C}(\text{CH}_3)_3$ ,  $-\text{CH}_2\text{CH}_2\text{C}(\text{CH}_2\text{CH}_3)_3$ ,  $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}(\text{CH}_3)_2$ ,  $-\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)_2$ ,  $-\text{CH}(\text{CH}_2\text{CH}_3)\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$ , and others. The phrase also includes

25 cyclic alkyl groups such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl and such rings substituted with straight and branched

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chain alkyl groups as defined above. The phrase also includes polycyclic alkyl groups such as, but not limited to, adamantyl norbornyl, and bicyclo[2.2.2]octyl and such rings substituted with straight and branched chain alkyl groups as defined above. Thus, the phrase unsubstituted alkyl groups includes primary alkyl groups, 5 secondary alkyl groups, and tertiary alkyl groups. Unsubstituted alkyl groups may be bonded to one or more carbon atom(s), oxygen atom(s), nitrogen atom(s), and/or sulfur atom(s) in the parent compound. Preferred unsubstituted alkyl groups include straight and branched chain alkyl groups and cyclic alkyl groups having 1 to 20 carbon atoms. More preferred such unsubstituted alkyl groups have from 1 to 10 10 carbon atoms while even more preferred such groups have from 1 to 5 carbon atoms. Most preferred unsubstituted alkyl groups include straight and branched chain alkyl groups having from 1 to 3 carbon atoms and include methyl, ethyl, propyl, and  $-\text{CH}(\text{CH}_3)_2$ .

The phrase "substituted alkyl" refers to an unsubstituted alkyl group 15 as defined above in which one or more bonds to a carbon(s) or hydrogen(s) are replaced by a bond to non-hydrogen and non-carbon atoms such as, but not limited to, a halogen atom in halides such as F, Cl, Br, and I; and oxygen atom in groups such as hydroxyl groups, alkoxy groups, aryloxy groups, and ester groups; a sulfur atom in groups such as thiol groups, alkyl and aryl sulfide groups, sulfone groups, 20 sulfonyl groups, and sulfoxide groups; a nitrogen atom in groups such as amines, amides, alkylamines, dialkylamines, arylamines, alkylarylamines, diarylamines, N-oxides, imides, and enamines; a silicon atom in groups such as in trialkylsilyl groups, dialkylarylsilyl groups, alkyl diarylsilyl groups, and triarylsilyl groups; and other heteroatoms in various other groups. Substituted alkyl groups also include 25 groups in which one or more bonds to a carbon(s) or hydrogen(s) atom is replaced by a bond to a heteroatom such as oxygen in carbonyl, carboxyl, and ester groups; nitrogen in groups such as imines, oximes, hydrazones, and nitriles. Preferred substituted alkyl groups include, among others, alkyl groups in which one or more bonds to a carbon or hydrogen atom is/are replaced by one or more bonds to 30 fluorine atoms. One example of a substituted alkyl group is the trifluoromethyl

group and other alkyl groups that contain the trifluoromethyl group. Other alkyl groups include those in which one or more bonds to a carbon or hydrogen atom is replaced by a bond to an oxygen atom such that the substituted alkyl group contains a hydroxyl, alkoxy, aryloxy group, or heterocyclyloxy group. Still other alkyl

5 groups include alkyl groups that have an amine, alkylamine, dialkylamine, arylamine, (alkyl)(aryl)amine, diarylamine, heterocyclylamine, (alkyl)(heterocyclyl)amine, (aryl)(heterocyclyl)amine, or diheterocyclylamine group.

The phrase "unsubstituted aryl" refers to aryl groups that do not contain heteroatoms. Thus the phrase includes, but is not limited to, groups such as

10 phenyl, biphenyl, anthracenyl, naphthenyl by way of example. Although the phrase "unsubstituted aryl" includes groups containing condensed rings such as naphthalene, it does not include aryl groups that have other groups such as alkyl or halo groups bonded to one of the ring members, as aryl groups such as tolyl are considered herein to be substituted aryl groups as described below. A preferred

15 unsubstituted aryl group is phenyl. Unsubstituted aryl groups may be bonded to one or more carbon atom(s), oxygen atom(s), nitrogen atom(s), and/or sulfur atom(s) in the parent compound, however.

The phrase "substituted aryl group" has the same meaning with respect to unsubstituted aryl groups that substituted alkyl groups had with respect to

20 unsubstituted alkyl groups. However, a substituted aryl group also includes aryl groups in which one of the aromatic carbons is bonded to one of the non-carbon or non-hydrogen atoms described above and also includes aryl groups in which one or more aromatic carbons of the aryl group is bonded to a substituted and/or unsubstituted alkyl, alkenyl, or alkynyl group as defined herein. This includes

25 bonding arrangements in which two carbon atoms of an aryl group are bonded to two atoms of an alkyl, alkenyl, or alkynyl group to define a fused ring system (e.g. dihydronaphthyl or tetrahydronaphthyl). Thus, the phrase "substituted aryl" includes, but is not limited to tolyl, and hydroxyphenyl among others.

The phrase "unsubstituted alkenyl" refers to straight and branched chain and cyclic groups such as those described with respect to unsubstituted alkyl groups as defined above, except that at least one double bond exists between two carbon atoms. Examples include, but are not limited to vinyl,  $-\text{CH}=\text{C}(\text{H})(\text{CH}_3)$ ,  
5  $-\text{CH}=\text{C}(\text{CH}_3)_2$ ,  $-\text{C}(\text{CH}_3)=\text{C}(\text{H})_2$ ,  $-\text{C}(\text{CH}_3)=\text{C}(\text{H})(\text{CH}_3)$ ,  $-\text{C}(\text{CH}_2\text{CH}_3)=\text{CH}_2$ , cyclohexenyl, cyclopentenyl, cyclohexadienyl, butadienyl, pentadienyl, and hexadienyl among others.

The phrase "substituted alkenyl" has the same meaning with respect to unsubstituted alkenyl groups that substituted alkyl groups had with respect to  
10 unsubstituted alkyl groups. A substituted alkenyl group includes alkenyl groups in which a non-carbon or non-hydrogen atom is bonded to a carbon double bonded to another carbon and those in which one of the non-carbon or non-hydrogen atoms is bonded to a carbon not involved in a double bond to another carbon.

The phrase "unsubstituted alkynyl" refers to straight and branched  
15 chain groups such as those described with respect to unsubstituted alkyl groups as defined above, except that at least one triple bond exists between two carbon atoms. Examples include, but are not limited to  $-\text{C}\equiv\text{C}(\text{H})$ ,  $-\text{C}\equiv\text{C}(\text{CH}_3)$ ,  $-\text{C}\equiv\text{C}(\text{CH}_2\text{CH}_3)$ ,  $-\text{C}(\text{H}_2)\text{C}\equiv\text{C}(\text{H})$ ,  $-\text{C}(\text{H})_2\text{C}\equiv\text{C}(\text{CH}_3)$ , and  $-\text{C}(\text{H})_2\text{C}\equiv\text{C}(\text{CH}_2\text{CH}_3)$  among others.

The phrase "substituted alkynyl" has the same meaning with respect  
20 to unsubstituted alkynyl groups that substituted alkyl groups had with respect to unsubstituted alkyl groups. A substituted alkynyl group includes alkynyl groups in which a non-carbon or non-hydrogen atom is bonded to a carbon triple bonded to another carbon and those in which a non-carbon or non-hydrogen atom is bonded to a carbon not involved in a triple bond to another carbon.

25 The phrase "unsubstituted aralkyl" refers to unsubstituted alkyl groups as defined above in which a hydrogen or carbon bond of the unsubstituted alkyl group is replaced with a bond to an aryl group as defined above. For example, methyl ( $-\text{CH}_3$ ) is an unsubstituted alkyl group. If a hydrogen atom of the

methyl group is replaced by a bond to a phenyl group, such as if the carbon of the methyl were bonded to a carbon of benzene, then the compound is an unsubstituted aralkyl group (*i.e.*, a benzyl group). Thus the phrase includes, but is not limited to, groups such as benzyl, diphenylmethyl, and 1-phenylethyl ( $-\text{CH}(\text{C}_6\text{H}_5)(\text{CH}_3)$ ) among  
5 others.

The phrase "substituted aralkyl" has the same meaning with respect to unsubstituted aralkyl groups that substituted aryl groups had with respect to unsubstituted aryl groups. However, a substituted aralkyl group also includes groups in which a carbon or hydrogen bond of the alkyl part of the group is  
10 replaced by a bond to a non-carbon or a non-hydrogen atom. Examples of substituted aralkyl groups include, but are not limited to,  $-\text{CH}_2\text{C}(=\text{O})(\text{C}_6\text{H}_5)$ , and  $-\text{CH}_2(2\text{-methylphenyl})$  among others.

The phrase "unsubstituted heterocyclyl" refers to both aromatic and nonaromatic ring compounds including monocyclic, bicyclic, and polycyclic ring  
15 compounds such as, but not limited to, quinuclidyl, containing 3 or more ring members of which one or more is a heteroatom such as, but not limited to, N, O, and S. Although the phrase "unsubstituted heterocyclyl" includes condensed heterocyclic rings such as benzimidazolyl, it does not include heterocyclyl groups that have other groups such as alkyl or halo groups bonded to one of the ring  
20 members as compounds such as 2-methylbenzimidazolyl are substituted heterocyclyl groups. Examples of heterocyclyl groups include, but are not limited to: unsaturated 3 to 8 membered rings containing 1 to 4 nitrogen atoms such as, but not limited to pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, dihydropyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl (e.g. 4H-1,2,4-triazolyl, 1H-1,2,3-  
25 triazolyl, 2H-1,2,3-triazolyl etc.), tetrazolyl, (e.g. 1H-tetrazolyl, 2H tetrazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 4 nitrogen atoms such as, but not limited to, pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl; condensed unsaturated heterocyclic groups containing 1 to 4 nitrogen atoms such as, but not limited to, indolyl, isoindolyl, indolinyl, indoliziny, benzimidazolyl, quinolyl,

isoquinolyl, indazolyl, benzotriazolyl; unsaturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms such as, but not limited to, oxazolyl, isoxazolyl, oxadiazolyl (e.g. 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 2 oxygen atoms  
5 and 1 to 3 nitrogen atoms such as, but not limited to, morpholinyl; unsaturated condensed heterocyclic groups containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, benzoxazolyl, benzoxadiazolyl, benzoxazinyl (e.g. 2H-1,4-benzoxazinyl etc.); unsaturated 3 to 8 membered rings containing 1 to 3 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, thiazolyl, isothiazolyl,  
10 thiadiazolyl (e.g. 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, thiazolodinyll; saturated and unsaturated 3 to 8 membered rings containing 1 to 2 sulfur atoms such as, but not limited to, thienyl, dihydrodithiinyll, dihydrodithionyl, tetrahydrothiophene,  
15 tetrahydrothiopyran; unsaturated condensed heterocyclic rings containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, benzothiazolyl, benzothiadiazolyl, benzothiazinyl (e.g. 2H-1,4-benzothiazinyl, etc.), dihydrobenzothiazinyl (e.g. 2H-3,4-dihydrobenzothiazinyl, etc.), unsaturated 3 to 8 membered rings containing oxygen atoms such as, but not limited to furyl;  
20 unsaturated condensed heterocyclic rings containing 1 to 2 oxygen atoms such as benzodioxolyl (e.g. 1,3-benzodioxoyl, etc.); unsaturated 3 to 8 membered rings containing an oxygen atom and 1 to 2 sulfur atoms such as, but not limited to, dihydrooxathiinyll; saturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 2 sulfur atoms such as 1,4-oxathiane; unsaturated condensed rings  
25 containing 1 to 2 sulfur atoms such as benzothiényll, benzodithiinyll; and unsaturated condensed heterocyclic rings containing an oxygen atom and 1 to 2 oxygen atoms such as benzoxathiinyll. Heterocyclyl group also include those described above in which one or more S atoms in the ring is double-bonded to one or two oxygen atoms (sulfoxides and sulfones). For example, heterocyclyl groups include  
30 tetrahydrothiophene, tetrahydrothiophene oxide, and tetrahydrothiophene 1,1-

dioxide. Preferred heterocyclyl groups contain 5 or 6 ring members. More preferred heterocyclyl groups include morpholine, piperazine, piperidine, pyrrolidine, imidazole, pyrazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, thiomorpholine, thiomorpholine in which the S atom of the thiomorpholine is  
5 bonded to one or more O atoms, pyrrole, homopiperazine, oxazolidin-2-one, pyrrolidin-2-one, oxazole, quinuclidine, thiazole, isoxazole, furan, and tetrahydrofuran.

The phrase "substituted heterocyclyl" refers to an unsubstituted heterocyclyl group as defined above in which one of the ring members is bonded to  
10 a non-hydrogen atom such as described above with respect to substituted alkyl groups and substituted aryl groups. Examples, include, but are not limited to, 2-methylbenzimidazolyl, 5-methylbenzimidazolyl, 5-chlorobenzthiazolyl, 1-methyl piperazinyl, and 2-chloropyridyl among others.

The phrase "unsubstituted heterocyclylalkyl" refers to unsubstituted  
15 alkyl groups as defined above in which a hydrogen or carbon bond of the unsubstituted alkyl group is replaced with a bond to a heterocyclyl group as defined above. For example, methyl (-CH<sub>3</sub>) is an unsubstituted alkyl group. If a hydrogen atom of the methyl group is replaced by a bond to a heterocyclyl group, such as if the carbon of the methyl were bonded to carbon 2 of pyridine (one of the carbons  
20 bonded to the N of the pyridine) or carbons 3 or 4 of the pyridine, then the compound is an unsubstituted heterocyclylalkyl group.

The phrase "substituted heterocyclylalkyl" has the same meaning with respect to unsubstituted heterocyclylalkyl groups that substituted aralkyl groups had with respect to unsubstituted aralkyl groups. However, a substituted  
25 heterocyclylalkyl group also includes groups in which a non-hydrogen atom is bonded to a heteroatom in the heterocyclyl group of the heterocyclylalkyl group such as, but not limited to, a nitrogen atom in the piperidine ring of a piperidinylalkyl group.



The phrase "unsubstituted alkylaminoalkyl" refers to an unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is replaced by a bond to a nitrogen atom that is bonded to a hydrogen atom and an unsubstituted alkyl group as defined above. For example, methyl (-CH<sub>3</sub>) is an unsubstituted alkyl group. If a hydrogen atom of the methyl group is replaced by a bond to a nitrogen atom that is bonded to a hydrogen atom and an ethyl group, then the resulting compound is -CH<sub>2</sub>-N(H)(CH<sub>2</sub>CH<sub>3</sub>) which is an unsubstituted alkylaminoalkyl group.

The phrase "substituted alkylaminoalkyl" refers to an unsubstituted alkylaminoalkyl group as defined above except where one or more bonds to a carbon or hydrogen atom in one or both of the alkyl groups is replaced by a bond to a non-carbon or non-hydrogen atom as described above with respect to substituted alkyl groups except that the bond to the nitrogen atom in all alkylaminoalkyl groups does not by itself qualify all alkylaminoalkyl groups as being substituted. However, substituted alkylaminoalkyl groups does include groups in which the hydrogen bonded to the nitrogen atom of the group is replaced with a non-carbon and non-hydrogen atom.

The phrase "unsubstituted dialkylaminoalkyl" refers to an unsubstituted alkyl group as defined above in which a carbon bond or hydrogen bond is replaced by a bond to a nitrogen atom which is bonded to two other similar or different unsubstituted alkyl groups as defined above.

The phrase "substituted dialkylaminoalkyl" refers to an unsubstituted dialkylaminoalkyl group as defined above in which one or more bonds to a carbon or hydrogen atom in one or more of the alkyl groups is replaced by a bond to a non-carbon and non-hydrogen atom as described with respect to substituted alkyl groups. The bond to the nitrogen atom in all dialkylaminoalkyl groups does not by itself qualify all dialkylaminoalkyl groups as being substituted.

The phrase "unsubstituted heterocycloxyalkyl" refers to an unsubstituted alkyl group as defined above in which a carbon bond or hydrogen

bond is replaced by a bond to an oxygen atom which is bonded to an unsubstituted heterocyclyl group as defined above.

The phrase "substituted heterocycloxyalkyl" refers to an unsubstituted heterocycloxyalkyl group as defined above in which a bond to a carbon or hydrogen group of the alkyl group of the heterocycloxyalkyl group is  
5 bonded to a non-carbon and non-hydrogen atom as described above with respect to substituted alkyl groups or in which the heterocyclyl group of the heterocycloxyalkyl group is a substituted heterocyclyl group as defined above.

The phrase "unsubstituted arylaminoalkyl" refers to an unsubstituted  
10 alkyl group as defined above in which a carbon bond or hydrogen bond is replaced by a bond to a nitrogen atom which is bonded to at least one unsubstituted aryl group as defined above.

The phrase "substituted arylaminoalkyl" refers to an unsubstituted arylaminoalkyl group as defined above except where either the alkyl group of the  
15 arylaminoalkyl group is a substituted alkyl group as defined above or the aryl group of the arylaminoalkyl group is a substituted aryl group except that the bonds to the nitrogen atom in all arylaminoalkyl groups does not by itself qualify all arylaminoalkyl groups as being substituted. However, substituted arylaminoalkyl groups does include groups in which the hydrogen bonded to the nitrogen atom of  
20 the group is replaced with a non-carbon and non-hydrogen atom.

The phrase "unsubstituted heterocyclylaminoalkyl" refers to an unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is replaced by a bond to a nitrogen atom which is bonded to at least one unsubstituted heterocyclyl group as defined above.

25 The phrase "substituted heterocyclylaminoalkyl" refers to unsubstituted heterocyclylaminoalkyl groups as defined above in which the heterocyclyl group is a substituted heterocyclyl group as defined above and/or the alkyl group is a substituted alkyl group as defined above. The bonds to the nitrogen

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atom in all heterocyclaminoalkyl groups does not by itself qualify all heterocyclaminoalkyl groups as being substituted. However, substituted heterocyclaminoalkyl groups do include groups in which the hydrogen bonded to the nitrogen atom of the group is replaced with a non-carbon and non-hydrogen atom.

The phrase "unsubstituted alkylaminoalkoxy" refers to an unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is replaced by a bond to an oxygen atom which is bonded to the parent compound and in which another carbon or hydrogen bond of the unsubstituted alkyl group is bonded to a nitrogen atom which is bonded to a hydrogen atom and an unsubstituted alkyl group as defined above.

The phrase "substituted alkylaminoalkoxy" refers to unsubstituted alkylaminoalkoxy groups as defined above in which a bond to a carbon or hydrogen atom of the alkyl group bonded to the oxygen atom which is bonded to the parent compound is replaced by one or more bonds to a non-carbon and non-hydrogen atoms as discussed above with respect to substituted alkyl groups and/or if the hydrogen bonded to the amino group is bonded to a non-carbon and non-hydrogen atom and/or if the alkyl group bonded to the nitrogen of the amine is bonded to a non-carbon and non-hydrogen atom as described above with respect to substituted alkyl groups. The presence of the amine and alkoxy functionality in all alkylaminoalkoxy groups does not by itself qualify all such groups as substituted alkylaminoalkoxy groups.

The phrase "unsubstituted dialkylaminoalkoxy" refers to an unsubstituted alkyl group as defined above in which a carbon or hydrogen bond is replaced by a bond to an oxygen atom which is bonded to the parent compound and in which another carbon or hydrogen bond of the unsubstituted alkyl group is bonded to a nitrogen atom which is bonded to two other similar or different unsubstituted alkyl groups as defined above.

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The phrase "substituted dialkylaminoalkoxy" refers to an unsubstituted dialkylaminoalkoxy group as defined above in which a bond to a carbon or hydrogen atom of the alkyl group bonded to the oxygen atom which is bonded to the parent compound is replaced by one or more bonds to a non-carbon and non-hydrogen atoms as discussed above with respect to substituted alkyl groups and/or if one or more of the alkyl groups bonded to the nitrogen of the amine is bonded to a non-carbon and non-hydrogen atom as described above with respect to substituted alkyl groups. The presence of the amine and alkoxy functionality in all dialkylaminoalkoxy groups does not by itself qualify all such groups as substituted dialkylaminoalkoxy groups.

The phrase "unsubstituted heterocyclyloxy" refers to a hydroxyl group (-OH) in which the bond to the hydrogen atom is replaced by a bond to a ring atom of an otherwise unsubstituted heterocyclyl group as defined above.

The phrase "substituted heterocyclyloxy" refers to a hydroxyl group (-OH) in which the bond to the hydrogen atom is replaced by a bond to a ring atom of an otherwise substituted heterocyclyl group as defined above.

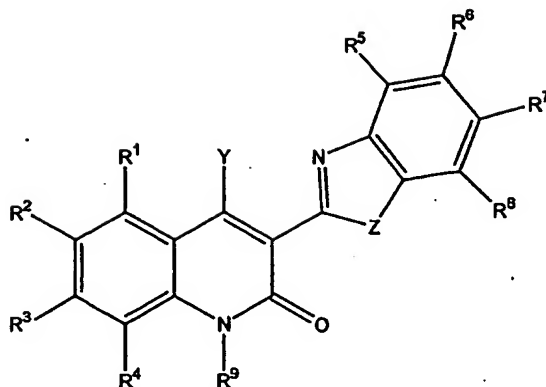
The term "protected" with respect to hydroxyl groups, amine groups, and sulfhydryl groups refers to forms of these functionalities which are protected from undesirable reaction with a protecting group known to those skilled in the art such as those set forth in Protective Groups in Organic Synthesis, Greene, T.W.; Wuts, P. G. M., John Wiley & Sons, New York, NY, (3rd Edition, 1999) which can be added or removed using the procedures set forth therein. Examples of protected hydroxyl groups include, but are not limited to, silyl ethers such as those obtained by reaction of a hydroxyl group with a reagent such as, but not limited to, t-butyldimethyl-chlorosilane, trimethylchlorosilane, triisopropylchlorosilane, triethylchlorosilane; substituted methyl and ethyl ethers such as, but not limited to methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, t-butoxymethyl ether, 2-methoxyethoxymethyl ether, tetrahydropyranyl ethers, 1-ethoxyethyl ether, allyl ether, benzyl ether; esters such as, but not limited to,

benzoylformate, formate, acetate, trichloroacetate, and trifluoroacetate. Examples of protected amine groups include, but are not limited to, amides such as, formamide, acetamide, trifluoroacetamide, and benzamide; imides, such as phthalimide, and dithiosuccinimide; and others. Examples of protected sulfhydryl groups include, but  
5 are not limited to, thioethers such as S-benzyl thioether, and S-4-picolyl thioether; substituted S-methyl derivatives such as hemithio, dithio and aminothio acetals; and others.

A "pharmaceutically acceptable salt" includes a salt with an inorganic base, organic base, inorganic acid, organic acid, or basic or acidic amino acid. As  
10 salts of inorganic bases, the invention includes, for example, alkali metals such as sodium or potassium; alkaline earth metals such as calcium and magnesium or aluminum; and ammonia. As salts of organic bases, the invention includes, for example, trimethylamine, triethylamine, pyridine, picoline, ethanolamine, diethanolamine, and triethanolamine. As salts of inorganic acids, the instant  
15 invention includes, for example, hydrochloric acid, hydroboric acid, nitric acid, sulfuric acid, and phosphoric acid. As salts of organic acids, the instant invention includes, for example, formic acid, acetic acid, trifluoroacetic acid, fumaric acid, oxalic acid, tartaric acid, maleic acid, citric acid, succinic acid, malic acid, methanesulfonic acid, benzenesulfonic acid, and p-toluenesulfonic acid. As salts of  
20 basic amino acids, the instant invention includes, for example, arginine, lysine and ornithine. Acidic amino acids include, for example, aspartic acid and glutamic acid.

Generally, the invention provides compounds including having the structure I. The invention also provides tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically  
25 acceptable salts of the tautomers. Structure I has the following formula:

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I

Preferred compounds having structure I are those within one of four groups.

In the first group of compounds:

5 Y is selected from  $-OR^{10}$  groups,  $-C(=O)-R^{11}$  groups,  $-NR^{12}R^{13}$  groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups,  
 10 substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclaminoalkyl groups, substituted or unsubstituted saturated heterocycl groups, substituted or unsubstituted heterocycloxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, or substituted or unsubstituted aryloxyalkyl groups;

15 Z is selected from O, S, or  $NR^{14}$  groups;

$R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  may be the same or different and are independently selected from H, Cl, Br, F, I,  $-CN$ ,  $-NO_2$ ,  $-OH$ ,  $-OR^{15}$  groups,  $-NR^{16}R^{17}$  groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or  
 20 tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or

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unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted  
 or unsubstituted heterocyclyl groups, substituted or unsubstituted aminoalkyl  
 groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or  
 unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl  
 5 groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or  
 unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted  
 heterocyclylalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl  
 groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups,  
 substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, or  $-C(=O)R^{18}$   
 10 groups;

$R^5$ ,  $R^6$ ,  $R^7$ , and  $R^8$  may be the same or different and are  
 independently selected from H, Cl, Br, F, I,  $-NO_2$ ,  $-OH$ ,  $-OR^{19}$  groups,  $-NR^{20}R^{21}$   
 groups,  $-SH$ ,  $-SR^{22}$  groups,  $-S(=O)R^{23}$  groups,  $-S(=O)_2R^{24}$  groups,  $-CN$ , substituted  
 or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups,  
 15 substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted  
 or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted  
 or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups,  
 substituted or unsubstituted heterocyclylalkyl groups,  $-C(=O)R^{25}$  groups, substituted  
 or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl  
 20 groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or  
 unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl  
 groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or  
 unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted  
 diheterocyclylaminoalkyl groups, substituted or unsubstituted  
 25 (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted  
 (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl  
 groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted  
 aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

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R<sup>9</sup> and R<sup>14</sup> may be the same or different and are independently selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R<sup>10</sup> is selected from substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups, -NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl), -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, or substituted or unsubstituted heterocyclylalkyl groups;

R<sup>11</sup> is selected from H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl) groups, -O-alkyl groups, O-aryl groups, heterocycliloxyalkyl groups, or substituted or unsubstituted aryl groups;

R<sup>12</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R<sup>13</sup> is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl



groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted heterocyclalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocycl groups, -C(=O)-O-heterocycl groups, -C(=O)NH(heterocycl) groups, -C(=O)-N(heterocycl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocycl) groups, substituted or unsubstituted heterocyclaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted heterocycloxyalkyl groups, or -C(=O)-N(alkyl)(heterocycl) groups;

R<sup>15</sup> and R<sup>19</sup> may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocycl groups, substituted or unsubstituted heterocyclalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -NH(heterocycl) groups, -N(heterocycl)<sub>2</sub> groups, -N(alkyl)(heterocycl) groups, -N(aryl)(heterocycl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted

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heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyoxyalkyl groups;

$R^{16}$  and  $R^{20}$  may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

$R^{17}$  and  $R^{21}$  may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted

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aryloxyalkyl groups, substituted or unsubstituted heterocycloxyalkyl groups, or  
-C(=O)-N(alkyl)(heterocyclyl) groups;

R<sup>18</sup>, R<sup>23</sup>, R<sup>24</sup>, and R<sup>25</sup> may be the same or different and are  
independently selected from H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups,  
5 -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl)  
groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,  
-N(heterocyclyl)<sub>2</sub> groups, substituted or unsubstituted alkyl groups, substituted or  
unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups,  
substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryloxy  
10 groups, heterocycloxy groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups,  
-N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, or  
-N(aryl)O-aryl groups; and

R<sup>22</sup> is selected from substituted or unsubstituted alkyl groups,  
substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl  
15 groups.

In other embodiments of the invention, compounds of formula I  
above include a second group of compounds having the substituents described  
below:

Y is selected from -OR<sup>10</sup> groups, -C(=O)-R<sup>11</sup> groups, -NR<sup>12</sup>R<sup>13</sup>  
20 groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted  
heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups,  
substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted  
arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups,  
substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or  
25 unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted saturated  
heterocyclyl groups, substituted or unsubstituted heterocycloxyalkyl groups,  
substituted or unsubstituted hydroxyalkyl groups, or substituted or unsubstituted  
aryloxyalkyl groups;

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Z is selected from O, S, or  $\text{NR}^{14}$  groups;

$\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , and  $\text{R}^4$  may be the same or different and are independently selected from H, Cl, Br, F, I,  $-\text{CN}$ ,  $-\text{NO}_2$ ,  $-\text{OH}$ ,  $-\text{OR}^{15}$  groups,  $-\text{NR}^{16}\text{R}^{17}$  groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, and tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, or  $-\text{C}(=\text{O})\text{R}^{18}$  groups;

$\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ , and  $\text{R}^8$  may be the same or different and are independently selected from H, Cl, Br, F, I,  $-\text{NO}_2$ ,  $-\text{OH}$ ,  $-\text{OR}^{19}$  groups,  $-\text{NR}^{20}\text{R}^{21}$  groups,  $-\text{SH}$ ,  $-\text{SR}^{22}$  groups,  $-\text{S}(=\text{O})\text{R}^{23}$  groups,  $-\text{S}(=\text{O})_2\text{R}^{24}$  groups,  $-\text{CN}$ , substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, and tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups,  $-\text{C}(=\text{O})\text{R}^{25}$  groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycliloxyalkyl groups;

R<sup>9</sup> is selected from the group consisting of -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R<sup>10</sup> is selected from substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, or substituted or unsubstituted heterocyclylalkyl groups;

R<sup>11</sup> is selected from H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, -O-alkyl groups, O-aryl groups, substituted or unsubstituted alkyl groups, or substituted or unsubstituted aryl groups;

R<sup>12</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R<sup>13</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or

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unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups,  
 substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl  
 groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups,  
 -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub>  
 5 groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted or  
 unsubstituted heterocyclalkyl groups, substituted or unsubstituted aminoalkyl  
 groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or  
 unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl  
 groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or  
 10 unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocycl groups, -C(=O)-  
 O-heterocycl groups, -C(=O)NH(heterocycl) groups, -C(=O)N(heterocycl)<sub>2</sub>  
 groups, -C(=O)N(aryl)(heterocycl) groups, -C(=O)N(alkyl)(heterocycl) groups,  
 substituted or unsubstituted heterocyclaminoalkyl groups, substituted or  
 unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups,  
 15 substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted  
 heterocycloxyalkyl groups;

R<sup>14</sup> is selected from H, -OH, substituted or unsubstituted alkoxy  
 groups, substituted or unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted or  
 unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups,  
 20 substituted or unsubstituted dialkylamino groups, substituted or unsubstituted  
 diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups,  
 substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups,  
 -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R<sup>15</sup> and R<sup>19</sup> may be the same or different and are independently  
 25 selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted  
 aryl groups, substituted or unsubstituted heterocycl groups, substituted or  
 unsubstituted heterocyclalkyl groups, -C(=O)H, -C(=O)-alkyl groups,  
 -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)  
 groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl)

groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted  
 alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups,  
 substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted  
 diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl  
 5 groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or  
 unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted  
 (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted  
 (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups,  
 substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted  
 10 aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

$R^{16}$  and  $R^{20}$  may be the same or different and are independently  
 selected from H, substituted or unsubstituted alkyl groups, substituted or  
 unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

$R^{17}$  and  $R^{21}$  may be the same or different and are independently  
 15 selected from H, substituted or unsubstituted alkyl groups, substituted or  
 unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups,  
 $-C(=O)H$ ,  $-C(=O)$ -alkyl groups,  $-C(=O)$ -aryl groups,  $-C(=O)NH_2$ ,  
 $-C(=O)NH$ (alkyl) groups,  $-C(=O)NH$ (aryl) groups,  $-C(=O)N$ (alkyl)<sub>2</sub> groups,  
 $-C(=O)N$ (aryl)<sub>2</sub> groups,  $-C(=O)N$ (alkyl)(aryl) groups,  $-C(=O)O$ -alkyl groups,  
 20  $-C(=O)O$ -aryl groups, substituted or unsubstituted heterocyclylalkyl groups,  
 substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted  
 alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups,  
 substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted  
 diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl  
 25 groups,  $-C(=O)$ -heterocyclyl groups,  $-C(=O)-O$ -heterocyclyl groups,  
 $-C(=O)NH$ (heterocyclyl) groups,  $-C(=O)-N$ (heterocyclyl)<sub>2</sub> groups,  
 $-C(=O)N$ (aryl)(heterocyclyl) groups,  $-C(=O)-N$ (alkyl)(heterocyclyl) groups,  
 substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or  
 unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups,

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substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups;

$R^{18}$ ,  $R^{23}$ ,  $R^{24}$ , and  $R^{25}$  may be the same or different and are independently selected from H,  $-NH_2$ ,  $-NH(alkyl)$  groups,  $-NH(aryl)$  groups,  $-N(alkyl)_2$  groups,  $-N(aryl)_2$  groups,  $-N(alkyl)(aryl)$  groups,  $-NH(heterocyclyl)$  groups,  $-N(heterocyclyl)(alkyl)$  groups,  $-N(heterocyclyl)(aryl)$  groups,  $-N(heterocyclyl)_2$  groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups,  $-OH$ , substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryloxy groups,  $-NHOH$ ,  $-N(alkyl)OH$  groups,  $-N(aryl)OH$  groups,  $-N(alkyl)O-alkyl$  groups,  $-N(aryl)O-alkyl$  groups,  $-N(alkyl)O-aryl$  groups, or  $-N(aryl)O-aryl$  groups; and

$R^{22}$  is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

In another embodiment, the present invention provides a third group of compounds having the general formula I above with substituents selected from the following:

Y is selected from  $-OH$ ,  $SH$ , alkylthio groups, arylthio groups,  $-OR^{10}$  groups,  $-C(=O)-R^{11}$  groups,  $-NR^{12}R^{13}$  groups,  $-CN$ , substituted or unsubstituted alkyl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted  $(alkyl)(aryl)aminoalkyl$  groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups,



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substituted or unsubstituted heterocycloxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, or substituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or  $\text{NR}^{14}$  groups;

5  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , and  $\text{R}^4$  may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or  
10 unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or  
15 unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclalkyl groups, or -C(=O)R<sup>18</sup>;

$\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ , and  $\text{R}^8$  may be the same or different and are independently selected from H, Cl, Br, F, I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups, -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted  
20 or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted  
25 dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclalkyl groups, -C(=O)R<sup>25</sup> groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclaminoalkyl groups, substituted or

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unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

$R^9$  and  $R^{14}$  may be the same or different and are independently  
5 selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups,  
10 substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

$R^{10}$  is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H,  
15 -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups, -C(=O)NH(heterocyclyl) groups,  
20 -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, or -C(=O)N(aryl)(heterocyclyl) groups;

$R^{11}$  is selected from H, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, -NH(heterocyclyl)  
25 groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, or substituted or unsubstituted aryl groups;

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$R^{12}$  is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

$R^{13}$  is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

$R^{15}$  and  $R^{19}$  may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl)

groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

R<sup>16</sup> and R<sup>20</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R<sup>17</sup> and R<sup>21</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups,

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substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;

$R^{18}$ ,  $R^{23}$ ,  $R^{24}$ , and  $R^{25}$  may be the same or different and are independently selected from H,  $-NH_2$ ,  $-NH(alkyl)$  groups,  $-NH(aryl)$  groups,  $-N(alkyl)_2$  groups,  $-N(aryl)_2$  groups,  $-N(alkyl)(aryl)$  groups,  $-NH(heterocyclyl)$  groups,  $-N(heterocyclyl)(alkyl)$  groups,  $-N(heterocyclyl)(aryl)$  groups,  $-N(heterocyclyl)_2$  groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups,  $-OH$ , substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyl groups,  $-NHOH$ ,  $-N(alkyl)OH$  groups,  $-N(aryl)OH$  groups,  $-N(alkyl)O-alkyl$  groups,  $-N(aryl)O-alkyl$  groups,  $-N(alkyl)O-aryl$  groups, or  $-N(aryl)O-aryl$  groups; and

$R^{22}$  is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups.

In the third group of compounds, at least one of  $R^5$ ,  $R^6$ ,  $R^7$ , or  $R^8$  is selected from substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted saturated heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted  $(alkyl)(aryl)aminoalkyl$  groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups;  $-OR^{19}$  groups where  $R^{19}$  is selected from substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups,  $-C(=O)H$ ,  $-C(=O)-aryl$  groups,  $-C(=O)NH_2$ ,  $-C(=O)NH(alkyl)$  groups,

- C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclaminoalkyl groups, substituted or unsubstituted diheterocyclaminoalkyl groups, substituted or unsubstituted (heterocycl)(alkyl)aminoalkyl groups, substituted or unsubstituted (heterocycl)(aryl)aminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted and unsubstituted heterocycloxyalkyl groups; -NR<sup>20</sup>R<sup>21</sup> groups where R<sup>20</sup> is selected from substituted or unsubstituted heterocycl groups; -NR<sup>20</sup>R<sup>21</sup> groups where R<sup>21</sup> is selected from substituted or unsubstituted heterocycl groups, -C(=O)H, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted heterocyclalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups; or -C(=O)R<sup>25</sup> groups where R<sup>25</sup> is selected from H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -NH(heterocycl) groups, -N(heterocycl)(alkyl) groups, -N(heterocycl)(aryl) groups, -N(heterocycl)<sub>2</sub> groups, substituted or unsubstituted aryl groups, substituted or unsubstituted aryloxy groups, or substituted or unsubstituted heterocycl groups.

In yet another embodiment, the present invention encompasses compounds of formula I in which the substituents described below define a fourth group of compounds:

Y is selected from -OH, SH, alkylthio groups, arylthio groups, -OR<sup>10</sup> groups, -C(=O)-R<sup>11</sup> groups, -NR<sup>12</sup>R<sup>13</sup> groups, -CN, substituted or unsubstituted alkyl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclaminoalkyl groups, substituted or unsubstituted heterocycl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocycloxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, or substituted or unsubstituted aryloxyalkyl groups;

Z is selected from O, S, or NR<sup>14</sup> groups;

R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> may be the same or different and are independently selected from H, Cl, Br, F, I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocycl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclalkyl groups, or -C(=O)R<sup>18</sup> groups;

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R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> may be the same or different and are independently selected from H, Cl, Br, F, I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups, -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted or unsubstituted amidinyl groups, substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary, secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)R<sup>25</sup> groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycliloxyalkyl groups;

R<sup>9</sup> and R<sup>14</sup> may be the same or different and are independently selected from H, -OH, substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups;

R<sup>10</sup> is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,



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-C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, or

5 -C(=O)N(aryl)(heterocyclyl) groups;

R<sup>11</sup> is selected from H, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, -NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, or substituted or

10 unsubstituted aryl groups;

R<sup>12</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

R<sup>13</sup> is selected from H, substituted or unsubstituted alkyl groups,

15 substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups,

20 substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups,

25 -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocyclyl) groups,

-C(=O)N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycliloxyalkyl groups;

- 5                   R<sup>15</sup> and R<sup>19</sup> may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl, substituted or unsubstituted diheterocyclylaminoalkyl, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl, substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycliloxyalkyl groups;

R<sup>16</sup> and R<sup>20</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl groups;

- 25                   R<sup>17</sup> and R<sup>21</sup> may be the same or different and are independently selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups,

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-C(=O)O-aryl groups, substituted or unsubstituted heterocyclylalkyl groups,  
 substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted  
 alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups,  
 substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted  
 5 diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl  
 groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups,  
 -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)<sub>2</sub> groups,  
 -C(=O)-N(alkyl)(heterocyclyl) groups, -C(=O)-N(aryl)(heterocyclyl) groups,  
 substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or  
 10 unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups,  
 substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted  
 heterocyclyloxyalkyl groups;

R<sup>18</sup>, R<sup>23</sup>, R<sup>24</sup>, and R<sup>25</sup> may be the same or different and are  
 independently selected from H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups,  
 15 -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl)  
 groups, -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,  
 -N(heterocyclyl)<sub>2</sub> groups, substituted or unsubstituted alkyl groups, substituted or  
 unsubstituted aryl groups, -OH, substituted or unsubstituted alkoxy groups,  
 substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyl  
 20 groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl  
 groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, or -N(aryl)O-aryl groups;  
 and

R<sup>22</sup> is selected from substituted or unsubstituted alkyl groups,  
 substituted or unsubstituted aryl groups, or substituted or unsubstituted heterocyclyl  
 25 groups.

In the fourth group of compounds, at least one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, or R<sup>4</sup> is  
 an -OR<sup>15</sup> group and R<sup>15</sup> is selected from substituted or unsubstituted  
 heterocyclylalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups,  
 substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted

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aminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted diheterocyclylaminoalkyl groups, substituted or unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, or substituted or unsubstituted (heterocyclyl)(aryl)aminoalkyl groups.

In the first, second, or third group of compounds Z is preferably an  $-NR^{14}$  group, more preferably where  $R^{14}$  is H. Preferred compounds of the fourth group include those compounds in which Z is an  $-NR^{10}$  group, more preferably where  $R^{10}$  is H.

Y is preferably an  $-OR^{10}$  group, an  $-NR^{12}R^{13}$  group, or a substituted or unsubstituted alkynyl group, or more preferably is an  $-NR^{12}N^{13}$  group in the first, second, third, and fourth groups of compounds. In more preferred compounds of the first group, Y is a  $NR^{12}R^{13}$  group and  $R^{12}$  is H. In more preferred compounds of the second and third groups, Y is a  $NR^{12}R^{13}$  group and one or both of  $R^{12}$  and  $R^{13}$  are H.

Other preferred compounds of the first, second, and third groups include those where Y is selected from  $-N(CH_3)_2$ ,  $-NH(CH_3)$ ,  $-NH(CH_2CH_3)$ ,  $-N(CH_2CH_3)_2$ ,  $-NH(aryl)$  groups,  $-N(aryl)_2$  groups,  $-NHNH_2$ ,  $-NHN(CH_3)_2$ ,  $-N(CH_3)NH(CH_3)$ ,  $-NH(CH_2)_mNH_2$  groups,  $-NH(CH_2)_mNH(alkyl)$  groups,  $-NH(CH_2)_mN(alkyl)_2$  groups,  $-N(alkyl)(CH_2)_mNH_2$  groups,  $-N(alkyl)(CH_2)_mNH(alkyl)$  groups,  $-N(alkyl)(CH_2)_mN(alkyl)_2$  groups,  $-NH(CH_2)_m(heterocyclyl)$  groups,  $-N(alkyl)[(CH_2)_m(heterocyclyl)]$  groups,  $-NH(CH_2)_mOH$  groups,  $-NH(CH_2)_mOCH_3$  groups,  $-NHCH_2CH(NH_2)CH(CH_3)_2$ ,  $-NH(2\text{-aminocyclohexyl})$ ,  $-NH(cyclohexyl)$ ,  $-NHOCH_3$ ,  $-NH(N\text{-morpholinyl})$ ,  $-NH(quinuclidyl)$ , especially  $-NH(quinuclid-3\text{-yl})$ , or groups where  $R^{12}$  and  $R^{13}$  join to form a substituted or unsubstituted saturated 5 or 6 membered N-containing ring,

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where m is an integer ranging from 2 to 4 such as 2, 3, or 4 and n is an integer ranging from 0 to 3 such as 0, 1, 2, or 3.

More preferred compounds of the first, second, and third also include those in which Y is selected from -NH(5-benzimidazolyl), -NH(CH<sub>2</sub>)<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, -  
 5 NH(CH<sub>2</sub>)<sub>2</sub>OH, -NH(CH<sub>2</sub>)(4-imidazolyl), -NH(CH<sub>2</sub>)(3-imidazolyl), -NH(CH<sub>2</sub>)(4-pyridyl), -NH(CH<sub>2</sub>)(2-pyridyl), -NH(CH<sub>2</sub>)(3-pyridyl), -NH(CH<sub>2</sub>)(2-tetrahydrofuranyl), -NH(CH<sub>2</sub>)(4-piperidinyl), -NH(CH<sub>2</sub>)(3-piperidinyl), -  
 NH(CH<sub>2</sub>)<sub>2</sub>[2-(N-methylpyrrolidinyl)], -NH(CH<sub>2</sub>)<sub>2</sub>(2-pyrrolidinyl), -NH(CH<sub>2</sub>)[2-(N-methylpyrrolidinyl)], -NH(CH<sub>2</sub>)(2-pyrrolidinyl), -NH(3-piperidinyl), or -NH(3-pyrrolidinyl).  
 10 pyrrolidinyl).

Preferred compounds of the first and second groups include those compounds where R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> are all H. Other preferred compounds of the first, second, third, and fourth groups include those where R<sup>1</sup> is selected from H, substituted or unsubstituted alkoxy groups, substituted or  
 15 unsubstituted heterocyclalkoxy groups, substituted or unsubstituted heterocycloxy groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkyl-, heterocyclyl-, or aryl-aminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl  
 20 groups, substituted or unsubstituted alkyl- or aryl-aminoalkoxy groups, substituted or unsubstituted dialkylaminoalkoxy groups, or substituted or unsubstituted diarylaminoalkoxy groups. Still other compounds of the first, second, third, and fourth groups include those in which R<sup>1</sup> is selected from F, Cl, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclalkoxy groups,  
 25 substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkyl-, heterocyclyl-, or aryl-aminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylaminoalkoxy groups, substituted or unsubstituted

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arylaminoalkoxy groups, substituted or unsubstituted dialkylaminoalkoxy groups, substituted or unsubstituted diarylaminoalkoxy groups, or substituted or unsubstituted (alkyl)(aryl)aminoalkoxy groups. Particular examples include:

5 -OCH<sub>3</sub>, -OCH<sub>2</sub>CH<sub>2</sub>(N-morpholinyl), -N-morpholinyl, -N-cis-dialkylmorpholinyl, -N-(4-alkyl)piperazinyl, -OCH<sub>2</sub>CH<sub>2</sub>N(alkyl)<sub>2</sub> groups, -OCH<sub>2</sub>CH<sub>2</sub>NH(alkyl) groups, -OCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, -OCH<sub>2</sub>CH<sub>2</sub>NH(aryl) groups, -OCH<sub>2</sub>CH<sub>2</sub>N(aryl)<sub>2</sub> groups, -OCH<sub>2</sub>CH<sub>2</sub>N(alkyl)(aryl) groups, alkoxy groups, -O(4-piperidinyl), -O[4-(1-alkyl)piperidinyl] groups, -O[3-(1-alkyl)piperidinyl] groups, -O[3-quinolidinyl], -OCH<sub>2</sub>(2-pyridyl), -OCH<sub>2</sub>(4-pyridyl), -O(3-pyrrolidinyl), or -O[3-(1-

10 alkyl)pyrrolidinyl] groups.

Still other preferred compounds of the first, second, third, and fourth groups include those in which R<sup>2</sup> is selected from F, Cl, -NO<sub>2</sub>, -OCH<sub>3</sub>, N-morpholinyl, -N-cis-dialkylmorpholinyl, -N-(4-alkyl)piperazinyl, or -OCH<sub>2</sub>(2-pyridyl). Other preferred compounds of the first, second, third, and fourth groups

15 include those where R<sup>2</sup> is selected from H, F, Cl, -NO<sub>2</sub>, substituted or unsubstituted heterocyclalkoxy groups, or substituted or unsubstituted heterocycl groups. Yet other preferred compounds of the first, second, third, and fourth groups include those where R<sup>2</sup> is selected from F, Cl, -NO<sub>2</sub>, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclalkoxy groups, substituted or

20 unsubstituted heterocycl groups, substituted or unsubstituted alkyl-, heterocycl-, and aryl-aminoalkyl groups, substituted or unsubstituted dialkyl- and diaryl-aminoalkyl groups, substituted or unsubstituted alkylaryl-aminoalkyl groups, substituted or unsubstituted alkyl- and aryl-aminoalkoxy groups, substituted or unsubstituted dialkyl- and diaryl-aminoalkoxy groups, or substituted or unsubstituted

25 alkylaryl-aminoalkoxy groups.

Still further preferred compounds of the first, second, third, and fourth groups include those where R<sup>6</sup> is an alkyl group having from one to four carbon atoms. In other preferred compounds of the first, second, third, and fourth groups, R<sup>7</sup> is an alkyl group having from one to four carbon atoms. Still further

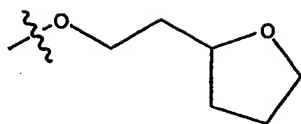
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preferred compounds of the four groups are those in which R<sup>6</sup> or R<sup>7</sup> is an -OR<sup>19</sup> group and R<sup>19</sup> is an alkyl group, an aryl group, a heterocyclyl group, or a heterocyclylalkyl group.

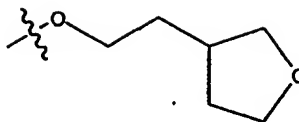
In still other preferred compounds of the first, second, third, and  
5 fourth groups, R<sup>6</sup> or R<sup>7</sup> is a -OCH<sub>2</sub>(CH<sub>2</sub>)<sub>q</sub>(heterocyclyl) group and q is 0, 1, 2, 3, or  
4, more preferably where the heterocyclyl group of the -OCH<sub>2</sub>(CH<sub>2</sub>)<sub>q</sub>(heterocyclyl)  
group is a heterocycle selected from substituted or unsubstituted morpholine,  
substituted or unsubstituted piperazine, substituted or unsubstituted piperidine,  
substituted or unsubstituted pyrrolidine, substituted or unsubstituted pyrrole,  
10 substituted or unsubstituted imidazole, substituted or unsubstituted pyrazole,  
substituted or unsubstituted 1,2,3-triazole, substituted or unsubstituted 1,2,4-  
triazole, substituted or unsubstituted tetrazole, substituted or unsubstituted  
thiomorpholine, substituted or unsubstituted homopiperazine, substituted or  
unsubstituted oxazolidin-2-one, substituted or unsubstituted pyrrolidin-2-one,  
15 substituted or unsubstituted pyridine, substituted or unsubstituted oxazole,  
substituted or unsubstituted isoxazole, substituted or unsubstituted thiazole,  
substituted or unsubstituted isothiazole, substituted or unsubstituted furan,  
substituted or unsubstituted thiophene, substituted or unsubstituted tetrahydrofuran,  
substituted or unsubstituted tetrahydrothiophene, substituted or unsubstituted  
20 benzimidazole, substituted or unsubstituted benzoxazole, or substituted or  
unsubstituted benzothiazole.

In groups including heterocyclyl groups, the heterocyclyl may be  
attached in various ways. For example, in the -OCH<sub>2</sub>(CH<sub>2</sub>)<sub>q</sub>(heterocyclyl) group,  
the heterocyclyl group may be bonded to a methylene carbon of the -OCH<sub>2</sub>(CH<sub>2</sub>)<sub>q</sub>  
25 group of the -OCH<sub>2</sub>(CH<sub>2</sub>)<sub>q</sub>(heterocyclyl) through various ring members. By way of  
non-limiting example, where q is 1 and the heterocyclyl group is tetrahydrofuran,  
the group could be represented by the formula -OCH<sub>2</sub>CH<sub>2</sub>(tetrahydrofuranyl) which  
corresponds to the following two structures:

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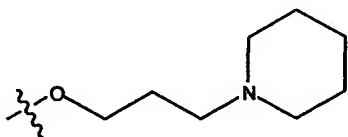


III

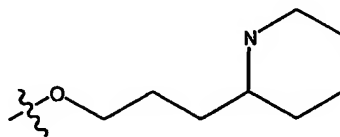


IV

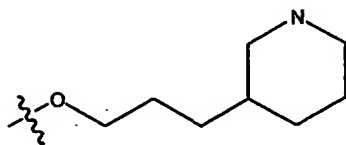
- where structure III represents the group that can be referred to as the  $-\text{OCH}_2\text{CH}_2(2\text{-tetrahydrofuranyl})$  group and structure IV represents the group that can be referred to as the  $-\text{OCH}_2\text{CH}_2(3\text{-tetrahydrofuranyl})$  group. When the
- 5 heterocyclyl group is a N-containing heterocycle, such as, but not limited to piperidine, piperazine, morpholine, or pyrrolidine, the heterocycle can be bonded to the methylene carbon through a ring carbon atom or through a nitrogen atom in the ring of the N-containing heterocycle. Both of these are preferred. Where the heterocyclyl group is a piperidine and q is 2 for an  $-\text{OCH}_2(\text{CH}_2)_q(\text{heterocyclyl})$
- 10 group, the following structures are possible and preferred:



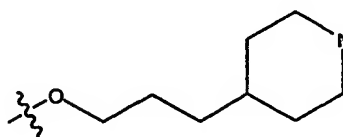
V



VI



VII

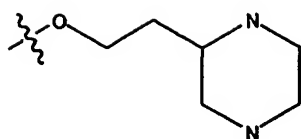


VIII

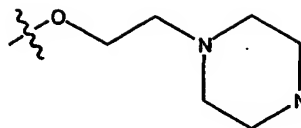
- Structure V is an example of a  $-\text{O}(\text{CH}_2)_3(\text{N-piperidinyl})$  or  $-\text{O}(\text{CH}_2)_3(1\text{-piperidinyl})$  group. Structure VI is an example of a  $-\text{O}(\text{CH}_2)_3(2\text{-piperidinyl})$  group. Structure VII is an example of a  $-\text{O}(\text{CH}_2)_3(3\text{-piperidinyl})$  group.
- 15 Structure VIII is an example of a  $-\text{O}(\text{CH}_2)_3(4\text{-piperidinyl})$  group. Where the heterocyclyl group is a piperazine and q is 1 for an  $-\text{OCH}_2(\text{CH}_2)_q(\text{heterocyclyl})$  group, the following structures are possible and preferred:



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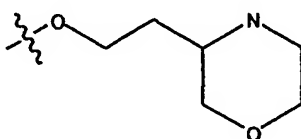


IX

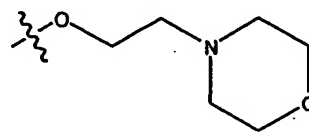


X

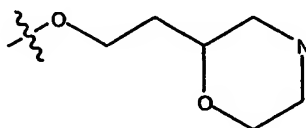
Structure IX is an example of a  $-\text{O}(\text{CH}_2)_2(2\text{-piperazinyl})$  group, and structure X is an example of a  $-\text{O}(\text{CH}_2)_2(1\text{-piperazinyl})$  or  $-\text{O}(\text{CH}_2)_2(\text{N-piperazinyl})$  group. Where the heterocyclyl group is a morpholine and q is 1 for an  $-\text{OCH}_2(\text{CH}_2)_q(\text{heterocyclyl})$  group, the following structures are possible and preferred:



XI



XII



XIII

Structure XI is an example of a  $-\text{O}(\text{CH}_2)_2(3\text{-morpholinyl})$  group, structure XII is an example of a  $-\text{O}(\text{CH}_2)_2(4\text{-morpholinyl})$  or  $-\text{O}(\text{CH}_2)_2(\text{N-morpholinyl})$  group, and structure XIII is an example of a  $-\text{O}(\text{CH}_2)_2(2\text{-morpholinyl})$  group. It will be observed that where the group is a pyrrolidine, and q is 1, the structures available include  $-\text{O}(\text{CH}_2)_2(1\text{-pyrrolidinyl})$  or  $-\text{O}(\text{CH}_2)_2(\text{N-pyrrolidinyl})$ ,  $-\text{O}(\text{CH}_2)_2(2\text{-pyrrolidinyl})$ , and  $-\text{O}(\text{CH}_2)_2(3\text{-pyrrolidinyl})$ .

Yet other preferred compounds of the first, second, third, and fourth groups include those where at least one of  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ , and  $\text{R}^8$  is a substituted or unsubstituted heterocyclyl group, more specifically a substituted or unsubstituted heterocyclyl group comprising at least one O or N atom, still more particularly a substituted or unsubstituted heterocyclyl group selected from morpholine, piperazine, piperidine, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyrrolidine, pyrazole, pyrrole, thiomorpholine, thiomorpholine in which the S atom of the

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thiomorpholine group is bonded to one or more O atoms, homopiperazine, benzimidazole, oxazolidin-2-one, pyrrolidin-2-one, imidazole, isoxazole, oxazole, isothiazole, thiazole, thiophene, furan, pyran, tetrahydrothiophene, tetrahydrofuran, tetrahydropyran, or pyridine.

- 5 Other preferred compounds of the first, second, third, and fourth groups include those in which at least one of R<sup>19</sup> or R<sup>21</sup> is selected from substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted
- 10 diarylaminoalkyl groups, (alkyl)(aryl)aminoalkyl groups, or substituted or unsubstituted heterocyclalkyl groups, including: -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>NH<sub>2</sub> groups, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>NH(alkyl) groups, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>NH(aryl) groups, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>N(alkyl)<sub>2</sub> groups, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>N(aryl)<sub>2</sub> groups, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>N(alkyl)(aryl) groups, or -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>(heterocycl) groups, wherein p is an integer ranging from 0 to 4 and
- 15 the heterocycl group of the -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>(heterocycl) group is a N-containing heterocycle selected from substituted or unsubstituted morpholine, substituted or unsubstituted pyrrolidine, substituted or unsubstituted piperazine, substituted or unsubstituted piperidine, substituted or unsubstituted pyrrole, substituted or unsubstituted imidazole, substituted or unsubstituted pyrazole, substituted or
- 20 unsubstituted 1,2,3-triazole, substituted or unsubstituted 1,2,4-triazole, substituted or unsubstituted tetrazole, substituted or unsubstituted thiomorpholine, substituted or unsubstituted homopiperazine, substituted or unsubstituted oxazolidin-2-one, substituted or unsubstituted pyrrolidin-2-one, substituted or unsubstituted pyridine, substituted or unsubstituted oxazole, substituted or unsubstituted isoxazole,
- 25 substituted or unsubstituted thiazole, substituted or unsubstituted isothiazole, substituted or unsubstituted benzimidazole, substituted or unsubstituted benzoxazole, or substituted or unsubstituted benzothiazole.

Still further preferred compounds according to the first, second, third, and fourth groups include those in which R<sup>25</sup> is selected from substituted or

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unsubstituted aryl groups, substituted or unsubstituted alkyl groups, -NH<sub>2</sub>,  
-NH(alkyl) groups, -N(alkyl)<sub>2</sub> groups, -NH(aryl) groups, -N(aryl)<sub>2</sub> groups,  
-N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups,  
-N(heterocyclyl)(aryl) groups, -N(heterocyclyl)<sub>2</sub> groups, or N-containing  
5 heterocycles. In such compounds, the N-containing heterocycles are bonded to the  
carbonyl carbon of the -C(=O)-R<sup>25</sup> group through either a nitrogen atom or a  
carbon atom in the rings of the N-containing heterocycles. In more preferred such  
compounds that are provided, the N-containing heterocycle of the R<sup>25</sup> group is  
selected from substituted or unsubstituted morpholine, substituted or unsubstituted  
10 pyrrolidine, substituted or unsubstituted piperazine, substituted or unsubstituted  
piperidine, substituted or unsubstituted pyrrole, substituted or unsubstituted  
imidazole, substituted or unsubstituted pyrazole, substituted or unsubstituted 1,2,3-  
triazole, substituted or unsubstituted 1,2,4-triazole, substituted or unsubstituted  
tetrazole, substituted or unsubstituted thiomorpholine, substituted or unsubstituted  
15 homopiperazine, substituted or unsubstituted oxazolidin-2-one, substituted or  
unsubstituted pyrrolidin-2-one, substituted or unsubstituted pyridine, substituted or  
unsubstituted oxazole, substituted or unsubstituted isoxazole, substituted or  
unsubstituted thiazole, substituted or unsubstituted isothiazole, substituted or  
unsubstituted benzimidazole, substituted or unsubstituted benzoxazole, or substituted  
20 or unsubstituted benzothiazole.

Preferred compounds according to the first, third, and fourth groups  
of compounds are also those where R<sup>9</sup> is H.

Preferred compounds of the fourth group of compounds include those  
where R<sup>1</sup> is an -OR<sup>15</sup> group and R<sup>15</sup> is selected from substituted or unsubstituted  
25 heterocyclylalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups,  
substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted  
aminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted  
or unsubstituted arylaminoalkyl groups, substituted or unsubstituted  
(alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclyl groups,

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substituted or unsubstituted heterocyclaminoalkyl groups, substituted or unsubstituted diheterocyclaminoalkyl groups, substituted or unsubstituted (heterocycl)(alkyl)aminoalkyl groups, or substituted or unsubstituted (heterocycl)(aryl)aminoalkyl groups.

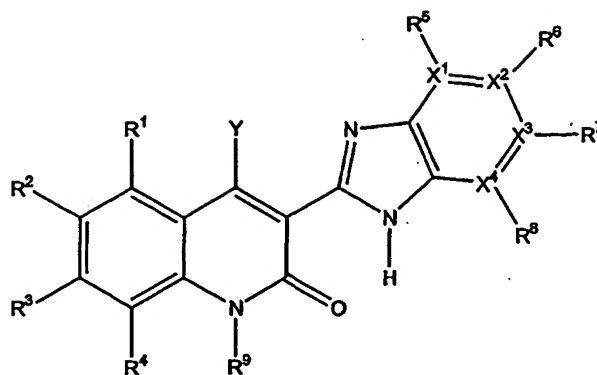
5           The invention provides a method of treating cancer, comprising administering to a patient a compound of formula I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer along with an anti-cancer drug selected from 5-FU or CPT-11. The compound of formula I may be selected from one of four groups or  
10   embodiments of the groups.

          The invention also provides the use of a compound of formula I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer in treating cancer in conjunction with an anti-cancer drug selected from 5-FU or CPT-11. The compound of formula  
15   I may be selected from one of four groups or embodiments of the groups.

          The invention also provides medicaments that include a compound of formula I, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer in treating cancer and an anti-cancer drug selected from 5-FU or CPT-11. The invention further  
20   provides for the use of such medicaments. The compound of formula I may be selected from any of four groups or embodiments of the groups.

          Other particularly preferred inhibitors of VEGF-RTK are compounds having the structure II, tautomers of the compounds, pharmaceutically acceptable salts of the compounds, and pharmaceutically acceptable salts of the tautomers.  
25   Structure II has the following formula:

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## II

- In compounds having structure II, Y is selected from H, -OH, -OR<sup>10</sup> groups, -SH, -SR<sup>11</sup> groups, -NR<sup>12</sup>R<sup>13</sup> groups, -CN, -C(=O)-R<sup>14</sup> groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted alkenyl groups,
- 5 substituted or unsubstituted alkynyl groups, substituted or unsubstituted aralkyl groups, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted
- 10 (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups.

- 15 In preferred compounds of structure II, Y is selected from H, -OH, -OR<sup>9</sup> groups, or -NR<sup>11</sup>R<sup>12</sup> groups. More preferably, Y is a -NR<sup>11</sup>R<sup>12</sup> group. Still more preferably, Y is a -NR<sup>11</sup>R<sup>12</sup> group and both R<sup>11</sup> and R<sup>12</sup> are hydrogen. In other preferred compounds having the structure II, Y is selected from -N(CH<sub>3</sub>)<sub>2</sub>, -NH(CH<sub>3</sub>), -NH(CH<sub>2</sub>CH<sub>3</sub>), -N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>, -NH(aryl) groups, -N(aryl)<sub>2</sub> groups,
- 20 -NHNH<sub>2</sub>, -NHN(CH<sub>3</sub>)<sub>2</sub>, -N(CH<sub>3</sub>)NH(CH<sub>3</sub>), -NH(CH<sub>2</sub>)<sub>m</sub>NH<sub>2</sub> groups, -NH(CH<sub>2</sub>)<sub>m</sub>NH(alkyl) groups, -NH(CH<sub>2</sub>)<sub>m</sub>N(alkyl)<sub>2</sub> groups, -N(alkyl)(CH<sub>2</sub>)<sub>m</sub>NH<sub>2</sub> groups, -N(alkyl)(CH<sub>2</sub>)<sub>m</sub>NH(alkyl) groups, -N(alkyl)(CH<sub>2</sub>)<sub>m</sub>N(alkyl)<sub>2</sub> groups,

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- NH(CH<sub>2</sub>)<sub>n</sub>(heterocyclyl) groups, -N(alkyl)[(CH<sub>2</sub>)<sub>n</sub>(heterocyclyl)] groups,  
 -NH(CH<sub>2</sub>)<sub>m</sub>OH groups, -NH(CH<sub>2</sub>)<sub>m</sub>OCH<sub>3</sub> groups, -NHCH<sub>2</sub>CH(NH<sub>2</sub>)CH(CH<sub>3</sub>)<sub>2</sub>,  
 -NH(2-aminocyclohexyl), -NH(cyclohexyl), -NHOCH<sub>3</sub>, -NH(N-morpholiny),  
 -NH(quinuclidyl), especially -NH(quinuclid-3-yl), and groups where R<sup>11</sup> and R<sup>12</sup>  
 5 join to form a substituted or unsubstituted saturated 5 or 6 membered N-containing  
 ring, where m is 2, 3, or 4 and n is 0, 1, 2, or 3. Still more preferred compounds  
 of this type are those in which Y is selected from -NH(5-benzimidazolyl),  
 -NH(CH<sub>2</sub>)<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, -NH(CH<sub>2</sub>)<sub>2</sub>OH, -NH(CH<sub>2</sub>)(4-imidazolyl), -NH(CH<sub>2</sub>)(3-  
 imidazolyl), -NH(CH<sub>2</sub>)(4-pyridyl), -NH(CH<sub>2</sub>)(2-pyridyl), -NH(CH<sub>2</sub>)(3-pyridyl),  
 10 -NH(CH<sub>2</sub>)(2-tetrahydrofuranyl), -NH(CH<sub>2</sub>)(4-piperidiny), -NH(CH<sub>2</sub>)(3-piperidiny),  
 -NH(CH<sub>2</sub>)<sub>2</sub>[2-(N-methyl-pyrrolidiny)], -NH(CH<sub>2</sub>)<sub>2</sub>(2-pyrrolidiny), -NH(CH<sub>2</sub>)[2-(N-  
 methylpyrrolidiny)], -NH(CH<sub>2</sub>)(2-pyrrolidiny), -NH(3-piperidiny), or -NH(3-  
 pyrrolidiny).

- In compounds of structure II, X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup>, and X<sup>4</sup> are selected from C  
 15 or N and at least one of X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup>, and X<sup>4</sup> is N. In some preferred compounds of  
 structure II, X<sup>1</sup> is N, R<sup>5</sup> is absent or H, and X<sup>2</sup>, X<sup>3</sup>, and X<sup>4</sup> are all C. In other  
 preferred compounds of structure II, X<sup>2</sup> is N, R<sup>6</sup> is absent or H, and X<sup>1</sup>, X<sup>3</sup>, and X<sup>4</sup>  
 are C. In other preferred compounds of structure II, X<sup>3</sup> is N, R<sup>7</sup> is absent or H, and  
 X<sup>1</sup>, X<sup>2</sup>, and X<sup>4</sup> are all C. In still other preferred compounds of structure II, X<sup>4</sup> is N,  
 20 R<sup>8</sup> is absent or H, and X<sup>1</sup>, X<sup>2</sup>, and X<sup>3</sup> are all C.

- In compounds of structure II, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> may  
 be the same or different and are independently selected from H, Cl, Br, F, I, -NO<sub>2</sub>,  
 -CN, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, -C(=O)R<sup>18</sup> groups, -SH, -SR<sup>19</sup> groups, -  
 S(=O)R<sup>20</sup> groups, S(=O)<sub>2</sub>R<sup>21</sup> groups, substituted or unsubstituted amidinyl groups,  
 25 substituted or unsubstituted guanidinyl groups, substituted or unsubstituted primary,  
 secondary, or tertiary alkyl groups, substituted or unsubstituted aryl groups,  
 substituted or unsubstituted alkenyl groups, substituted or unsubstituted alkynyl  
 groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted  
 alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups,

substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted heterocyclalkyl groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted heterocyclaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycloxyalkyl groups. In compounds of structure II, R<sup>5</sup> is absent or is H if X<sup>1</sup> is N, R<sup>6</sup> is absent or is H if X<sup>2</sup> is N, R<sup>7</sup> is absent or is H if X<sup>3</sup> is N, and R<sup>8</sup> is absent or is H if X<sup>4</sup> is N.

Some preferred compounds have the structure II where at least one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, or R<sup>8</sup> is a substituted or unsubstituted heterocycl group, and, in more particular embodiments, a substituted or unsubstituted heterocycl group selected from morpholine, piperazine, piperidine, 1,2,3-triazole, 1,2,4-triazole, tetrazole, pyrrolidine, pyrazole, pyrrole, thiomorpholine, homopiperazine, benzimidazole, oxazolidin-2-one, pyrrolidin-2-one, imidazole, isoxazole, oxazole, isothiazole, thiazole, thiophene, furan, pyran, tetrahydrothiophene, tetrahydrofuran, tetrahydropyran, and pyridine.

Still other preferred compounds having structure II are those in which R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are H. In some preferred embodiments, R<sup>1</sup> is selected from H, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclalkoxy groups, substituted or unsubstituted heterocycloxy groups, substituted or unsubstituted heterocycl groups, substituted or unsubstituted alkyl-, heterocycl-, or aryl-aminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkyl- or aryl-aminoalkoxy groups, substituted or unsubstituted dialkylaminoalkoxy groups, or substituted or unsubstituted diarylaminoalkoxy groups. In other preferred compounds, R<sup>1</sup> is selected from F, Cl, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclalkoxy groups,

substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkyl-, heterocyclyl-, or aryl-aminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or  
5 unsubstituted alkylaminoalkoxy groups, substituted or unsubstituted arylaminoalkoxy groups, substituted or unsubstituted dialkylaminoalkoxy groups, substituted or unsubstituted diarylaminoalkoxy groups, or substituted or unsubstituted (alkyl)(aryl)aminoalkoxy groups. Particular examples include:  
-OCH<sub>3</sub>, -OCH<sub>2</sub>CH<sub>2</sub>(N-morpholinyl), -N-morpholinyl, -N-cis-dimethylmorpholinyl,  
10 -N-(4-alkyl)piperazinyl, -OCH<sub>2</sub>CH<sub>2</sub>N(alkyl)<sub>2</sub> groups, -OCH<sub>2</sub>CH<sub>2</sub>NH(alkyl) groups, -OCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, -OCH<sub>2</sub>CH<sub>2</sub>NH(aryl) groups, -OCH<sub>2</sub>CH<sub>2</sub>N(aryl)<sub>2</sub> groups, alkoxy groups, -OCH<sub>2</sub>CH<sub>2</sub>N(alkyl)(aryl) groups, -O(4-piperidinyl), -O[4-(1-alkyl)piperidinyl] groups, -O[3-(1-alkyl)piperidinyl] groups, -O[3-quinuclidinyl],  
-OCH<sub>2</sub>(2-pyridyl), -OCH<sub>2</sub>(4-pyridyl), -O(3-pyrrolidinyl), -O[3-(1-alkyl)pyrrolidinyl], or other -O(heterocyclyl) groups not listed in this paragraph.  
15

In other compounds having the structure II, R<sup>2</sup> is selected from F, Cl, -NO<sub>2</sub>, -OCH<sub>3</sub>, -N-morpholinyl, -N-cis-dialkylmorpholinyl, -N-(4-alkyl)piperazinyl, or -OCH<sub>2</sub>(2-pyridyl). In yet other compounds having the structure II, R<sup>2</sup> is selected from H, F, Cl, -NO<sub>2</sub>, substituted or unsubstituted heterocyclalkoxy groups, or  
20 substituted or unsubstituted heterocyclyl groups. Yet other preferred compounds having the structure II include those where R<sup>2</sup> is selected from F, Cl, -NO<sub>2</sub>, substituted or unsubstituted alkoxy groups, substituted or unsubstituted heterocyclalkoxy groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted alkyl-, heterocycl-, and aryl-aminoalkyl groups,  
25 substituted or unsubstituted dialkyl- and diaryl-aminoalkyl groups, substituted or unsubstituted alkylaryl-aminoalkyl groups, substituted or unsubstituted alkyl- and aryl-aminoalkoxy groups, substituted or unsubstituted dialkyl- and diaryl-aminoalkoxy groups, or substituted or unsubstituted alkylaryl-aminoalkoxy groups.



In some preferred compounds having structure II, at least two of  $X^1$ ,  $X^2$ ,  $X^3$ , and  $X^4$  are C and the corresponding substituents  $R^5$ ,  $R^6$ ,  $R^7$ , and  $R^8$  are hydrogen, and at least one of  $X^1$ ,  $X^2$ ,  $X^3$ , and  $X^4$  is N. In yet other preferred compounds having structure II, three of  $R^5$ ,  $R^6$ ,  $R^7$ , and  $R^8$  are hydrogen and one of  $X^1$ ,  $X^2$ ,  $X^3$ , and  $X^4$  is N. In still other more preferred compounds of structure II,  $R^6$ ,  $R^7$ , or both  $R^6$  and  $R^7$  are alkyl groups such as those having from one to four carbon atoms. In yet other preferred compounds of structure II,  $R^6$  or  $R^7$  is an  $-OR^{14}$  group and  $R^{14}$  is an alkyl, aryl, heterocyclyl, or heterocyclylalkyl group. In still further compounds of structure II,  $R^6$  or  $R^7$  is a  $-OCH_2(CH_2)_q$ (heterocyclyl) group and  $q$  is 0, 1, 2, 3, or 4. In more preferred compounds in which  $R^6$  or  $R^7$  is a  $-OCH_2(CH_2)_q$ (heterocyclyl) group, the heterocyclyl group of the  $-OCH_2(CH_2)_n$ (heterocyclyl) group is a heterocycle selected from substituted or unsubstituted morpholine, substituted or unsubstituted piperazine, substituted or unsubstituted piperidine, substituted or unsubstituted pyrrolidine, substituted or unsubstituted pyrrole, substituted or unsubstituted imidazole, substituted or unsubstituted pyrazole, substituted or unsubstituted 1,2,3-triazole, substituted or unsubstituted 1,2,4-triazole, substituted or unsubstituted tetrazole, substituted or unsubstituted thiomorpholine, substituted or unsubstituted thiomorpholine in which the S atom of the thiomorpholine group is bonded to one or more O atoms, substituted or unsubstituted homopiperazine, substituted or unsubstituted oxazolidin-2-one, substituted or unsubstituted pyrrolidin-2-one, substituted or unsubstituted pyridine, substituted or unsubstituted oxazole, substituted or unsubstituted isoxazole, substituted or unsubstituted thiazole, substituted or unsubstituted isothiazole, substituted or unsubstituted furan, substituted or unsubstituted thiophene, substituted or unsubstituted tetrahydrofuran, substituted or unsubstituted tetrahydrothiophene, substituted or unsubstituted benzimidazole, substituted or unsubstituted benzoxazole, or substituted or unsubstituted benzothiazole.

In compounds of structure II,  $R^9$  is selected from H,  $-OH$ , substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups,  $-NH_2$ , substituted or unsubstituted alkylamino groups, substituted or unsubstituted

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arylamino groups, substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl groups, or -C(=O)-aryl groups. One group of  
5 particularly preferred compounds of structure II are those in which R<sup>9</sup> is hydrogen.

In compounds of structure II, R<sup>10</sup> is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl  
10 groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups, -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups,  
15 -C(=O)N(alkyl)(heterocyclyl) groups, or -C(=O)N(aryl)(heterocyclyl) groups;

In compounds of structure II, R<sup>11</sup> and R<sup>19</sup> may be the same or different and are independently selected from substituted or unsubstituted alkyl groups, or substituted or unsubstituted aryl groups whereas R<sup>12</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or  
20 substituted or unsubstituted heterocyclyl groups.

In compounds of structure II, R<sup>13</sup> is selected from H, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted or unsubstituted heterocyclylalkyl groups, substituted or unsubstituted  
25 aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkylamino groups, substituted or unsubstituted arylamino groups,

substituted or unsubstituted dialkylamino groups, substituted or unsubstituted diarylamino groups, substituted or unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups, -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups, -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted or unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups, substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted aryloxyalkyl groups, or substituted or unsubstituted heterocycliloxyalkyl groups. R<sup>12</sup> and R<sup>13</sup> may join together to form a 5 to 7 membered saturated or unsaturated, substituted or unsubstituted N-containing ring.

In compounds of structure II, R<sup>14</sup> is selected from H, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, -NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, or -N(aryl)(heterocyclyl) groups.

In compounds of structure II, R<sup>15</sup> is selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or unsubstituted heterocyclyl groups, substituted or unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted or

unsubstituted heterocyclylaminoalkyl groups, substituted or unsubstituted  
 diheterocyclylaminoalkyl groups, substituted or unsubstituted  
 (heterocyclyl)(alkyl)aminoalkyl groups, substituted or unsubstituted  
 (heterocyclyl)(aryl)aminoalkyl groups, substituted or unsubstituted alkoxyalkyl  
 5 groups, substituted or unsubstituted aryloxyalkyl groups, substituted or unsubstituted  
 hydroxyalkyl groups, or substituted or unsubstituted heterocyclyloxyalkyl groups.

In compounds of structure II,  $R^{16}$  is selected from H, substituted or  
 unsubstituted alkyl groups, substituted or unsubstituted aryl groups, or substituted or  
 unsubstituted heterocyclyl groups whereas  $R^{17}$  is selected from H, substituted or  
 10 unsubstituted alkyl groups, substituted or unsubstituted aryl groups, substituted or  
 unsubstituted heterocyclyl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl groups,  $-C(=O)$ -aryl  
 groups,  $-C(=O)NH_2$ ,  $-C(=O)NH(alkyl)$  groups,  $-C(=O)NH(aryl)$  groups,  
 $-C(=O)N(alkyl)_2$  groups,  $-C(=O)N(aryl)_2$  groups,  $-C(=O)N(alkyl)(aryl)$  groups,  
 $-C(=O)O$ -alkyl groups,  $-C(=O)O$ -aryl groups, substituted or unsubstituted  
 15 aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted  
 or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted  
 arylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups,  
 substituted or unsubstituted (aryl)(alkyl)aminoalkyl groups, substituted or  
 unsubstituted heterocyclylalkyl groups,  $-C(=O)$ -heterocyclyl groups,  
 20  $-C(=O)$ -Oheterocyclyl groups,  $-C(=O)NH(heterocyclyl)$  groups,  
 $-C(=O)N(heterocyclyl)_2$  groups,  $-C(=O)-N(alkyl)(heterocyclyl)$  groups,  
 $-C(=O)N(aryl)(heterocyclyl)$  groups, substituted or unsubstituted  
 heterocyclylaminoalkyl groups, substituted or unsubstituted hydroxyalkyl groups,  
 substituted or unsubstituted alkoxyalkyl groups, substituted or unsubstituted  
 25 aryloxyalkyl groups, substituted or unsubstituted heterocyclyloxyalkyl groups,  $-OH$ ,  
 substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy  
 groups, or  $-NH_2$  groups.  $R^{16}$  and  $R^{17}$  may join together to form a 5 to 7 membered  
 saturated or unsaturated, substituted or unsubstituted N-containing ring.

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Finally, in compounds of structure II,  $R^{18}$ ,  $R^{20}$ , and  $R^{21}$  may be the same or different and are independently selected from H,  $-NH_2$ ,  $-NH(\text{alkyl})$  groups,  $-NH(\text{aryl})$  groups,  $-N(\text{alkyl})_2$  groups,  $-N(\text{aryl})_2$  groups,  $-N(\text{alkyl})(\text{aryl})$  groups, substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups, 5  $-OH$ , substituted or unsubstituted alkoxy groups, substituted or unsubstituted aryloxy groups, substituted or unsubstituted heterocyclyl groups,  $-NHOH$ ,  $-N(\text{alkyl})OH$  groups,  $-N(\text{aryl})OH$  groups,  $-N(\text{alkyl})O\text{-alkyl}$  groups,  $-N(\text{aryl})O\text{-alkyl}$  groups,  $-N(\text{alkyl})O\text{-aryl}$  groups, or  $-N(\text{aryl})O\text{-aryl}$  groups.

Compounds having the structure II may include those in which  $R^{18}$  is 10 selected from substituted or unsubstituted alkyl groups, substituted or unsubstituted aryl groups,  $-NH_2$ ,  $-NH(\text{alkyl})$  groups,  $-N(\text{alkyl})_2$  groups,  $-NH(\text{aryl})$  groups,  $-N(\text{aryl})_2$  groups,  $-N(\text{alkyl})(\text{aryl})$  groups,  $-NH(\text{heterocyclyl})$  groups,  $-N(\text{heterocyclyl})(\text{alkyl})$  groups,  $-N(\text{heterocyclyl})(\text{aryl})$  groups,  $-N(\text{heterocyclyl})_2$  groups, or N-containing heterocycles, and the N-containing heterocycles are bonded 15 to the carbonyl carbon of the  $-C(=O)-R^{18}$  group through either a nitrogen atom or a carbon atom in the rings of the N-containing heterocycles. In still more preferred compounds in which  $R^{18}$  is a N-containing heterocycle, the N-containing heterocycle of the  $R^{18}$  group is selected from substituted or unsubstituted morpholine, substituted or unsubstituted pyrrolidine, substituted or unsubstituted piperazine, substituted or 20 unsubstituted piperidine, substituted or unsubstituted pyrrole, substituted or unsubstituted imidazole, substituted or unsubstituted pyrazole, substituted or unsubstituted 1,2,3-triazole, substituted or unsubstituted 1,2,4-triazole, substituted or unsubstituted tetrazole, substituted or unsubstituted thiomorpholine, substituted or unsubstituted homopiperazine, substituted or unsubstituted oxazolidin-2-one, 25 substituted or unsubstituted pyrrolidin-2-one, substituted or unsubstituted pyridine, substituted or unsubstituted oxazole, substituted or unsubstituted isoxazole, substituted or unsubstituted thiazole, substituted or unsubstituted isothiazole, substituted or unsubstituted benzimidazole, substituted or unsubstituted benzoxazole, or substituted or unsubstituted benzothiazole.

Other preferred compounds having structure II are provided in which R<sup>15</sup> or R<sup>17</sup> is selected from substituted or unsubstituted aminoalkyl groups, substituted or unsubstituted alkylaminoalkyl groups, substituted or unsubstituted arylaminoalkyl groups, substituted or unsubstituted dialkylaminoalkyl groups, substituted or unsubstituted diarylaminoalkyl groups, substituted or unsubstituted (alkyl)(aryl)aminoalkyl groups, or substituted or unsubstituted heterocyclylaminoalkyl groups including: -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>NH<sub>2</sub> groups, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>NH(alkyl) groups, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>NH(aryl) groups, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>N(alkyl)<sub>2</sub> groups, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>N(aryl)<sub>2</sub> groups, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>N(alkyl)(aryl) groups, or -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>(heterocyclyl) groups, where p is an integer ranging from 0 to 4 and the heterocyclyl group of the -CH<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>(heterocyclyl) group is a N-containing heterocycle selected from substituted or unsubstituted morpholine, substituted or unsubstituted pyrrolidine, substituted or unsubstituted piperazine, substituted or unsubstituted piperidine, substituted or unsubstituted pyrrole, substituted or unsubstituted imidazole, substituted or unsubstituted pyrazole, substituted or unsubstituted 1,2,3-triazole, substituted or unsubstituted 1,2,4-triazole, substituted or unsubstituted tetrazole, substituted or unsubstituted thiomorpholine, substituted or unsubstituted homopiperazine, substituted or unsubstituted oxazolidin-2-one, substituted or unsubstituted pyrrolidin-2-one, substituted or unsubstituted pyridine, substituted or unsubstituted oxazole, substituted or unsubstituted isoxazole, substituted or unsubstituted thiazole, substituted or unsubstituted isothiazole, substituted or unsubstituted benzimidazole, substituted or unsubstituted benzoxazole, or substituted or unsubstituted benzothiazole.

The invention also provides a method of treating cancer, comprising administering to a patient a compound of formula II, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer along with an anti-cancer drug selected from 5-FU or CPT-11.

The invention also provides the use of a compound of formula II, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a

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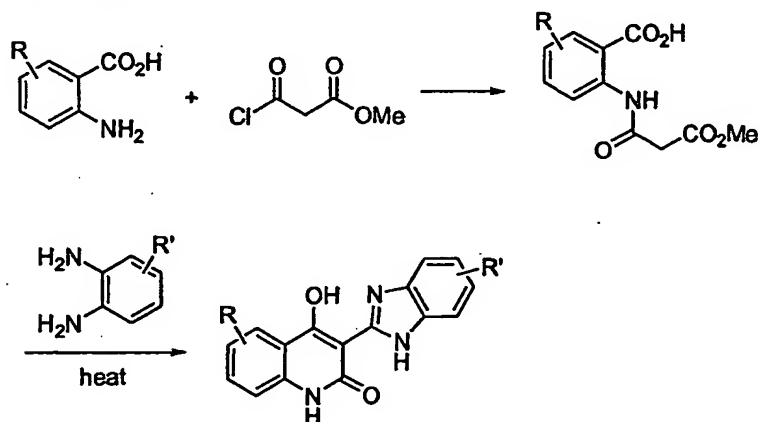
pharmaceutically acceptable salt of the tautomer in treating cancer in conjunction with an anti-cancer drug selected from 5-FU or CPT-11.

The invention also provides medicaments that include a compound of formula II, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer in treating cancer and an anti-cancer drug selected from 5-FU or CPT-11. The invention further provides for the use of such medicaments.

Compounds of structure I are readily synthesized from simple starting molecules as shown in the following Examples. Compounds of structure I may generally be prepared using benzene substituted with nitrile or carboxylic acid groups in addition to other optional groups.

Compounds of structure I may be synthesized from simple starting molecules as shown in Schemes 1-4 and exemplified in the Examples. As shown in Scheme 1, compounds of structure I may generally be prepared using aromatic compounds substituted with amines and carboxylic acid groups.

Scheme 1.



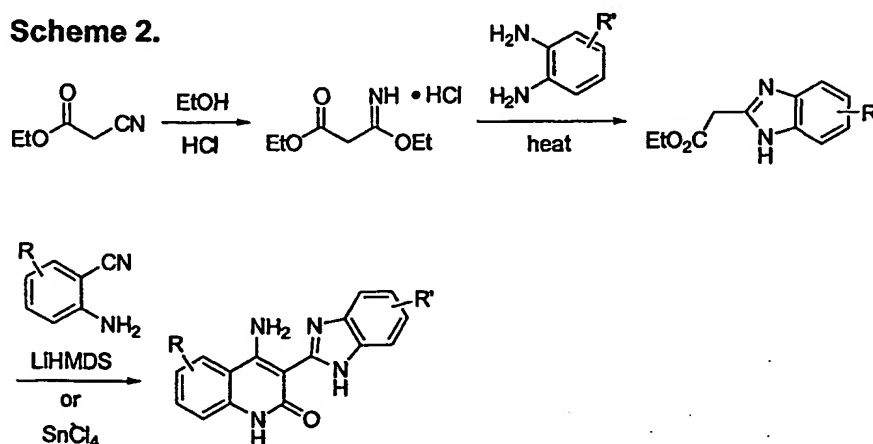
As shown in Scheme 1, a substituted aromatic compound such as a substituted or unsubstituted 2-aminobenzoic acid may be reacted with an acyl halide such as methyl 2-(chlorocarbonyl)acetate to produce an amide that will react with a substituted or unsubstituted 1,2-diaminobenzene. The resulting product is a 4-

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hydroxy-substituted compound of structure I. One skilled in the art will recognize that the procedure set forth in Scheme 1 may be modified to produce various compounds.

A method for preparing 4-amino substituted compounds of structure I is shown in Scheme 2. As shown in Scheme 2, aromatic compounds substituted with amine and nitrile groups may be used to synthesize 4-amino substituted compounds of structure I. A compound such as ethyl 2-cyanoacetate may be reacted with ethanol to produce ethyl 3-ethoxy-3-iminopropanoate hydrochloride. Subsequent reaction with a substituted or unsubstituted 1,2-phenylenediamine provides substituted or unsubstituted ethyl 2-benzimidazol-2-ylacetate. Reaction of a substituted or unsubstituted ethyl 2-benzimidazol-2-ylacetate with an aromatic compound having an amine and nitrile group such as substituted or unsubstituted 2-aminobenzonitrile with a base such as lithium bis(trimethylsilyl)amide or a Lewis acid such as tin tetrachloride provides the substituted or unsubstituted 4-amino substituted compound of structure I.

Scheme 2.

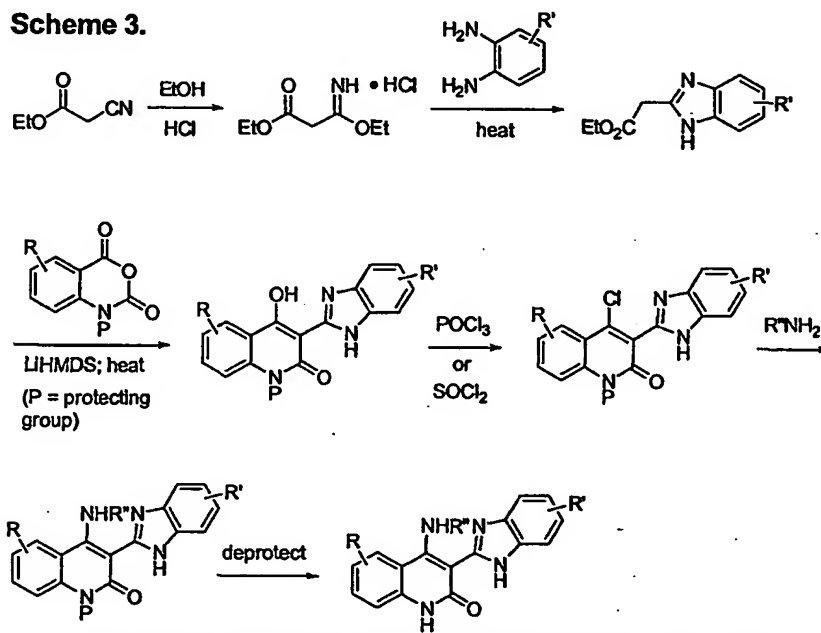


Scheme 3 illustrates a general synthetic route that allows for the synthesis of 4-dialkylamino and 4-alkylamino compounds of structure I. An inspection of Scheme 3 shows that 4-hydroxy substituted compounds of structure I may be converted into the 4-chloro derivative by reaction with phosphorous oxychloride or thionyl chloride. The 4-chloro derivative may then be reacted with an alkylamine or dialkylamine to produce the corresponding 4-alkylamino or 4-

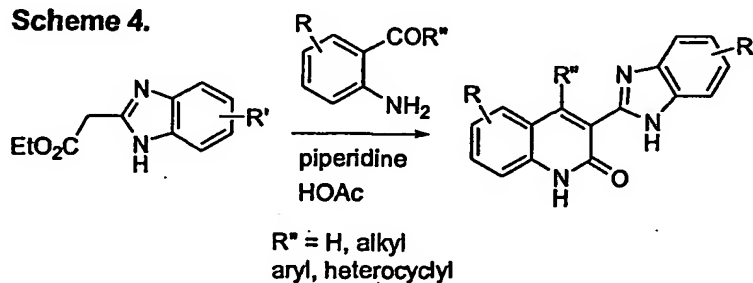


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dialkylamino derivative. Deprotection affords the final 4-alkylamino or 4-dialkylamino compounds of structure I. Other groups that may be reacted with the 4-chloro derivative in this manner include, but are not limited to, ROH, RSH, and CuCN.

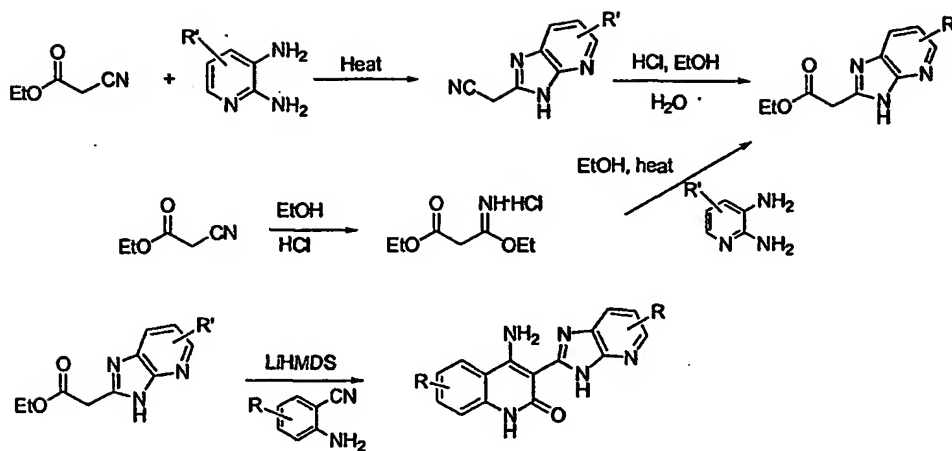
**Scheme 3.**

As shown in Scheme 4, the synthesis of compounds of structure I having a H, alkyl group, aryl group, or heterocyclyl group in the 4-position may be accomplished using a substituted or unsubstituted 2-benzimidazol-2-ylacetate prepared as shown in Schemes 2 and 3.

**Scheme 4.**

Heteroaromatic diamines may be used as precursors of compounds of structure II. The synthesis of compounds of structure II where Y = NH<sub>2</sub> is depicted in Scheme 5.

Scheme 5.



A compound such as ethyl cyanoacetate may be condensed with a substituted or unsubstituted heterocycle containing two ortho amino groups such as substituted or unsubstituted 1,2-diaminopyridine to obtain a substituted or unsubstituted 2-imidazolo[5,4-b]pyridin-2-ylacetate, which may subsequently be hydrolyzed in acidic medium to provide a substituted or unsubstituted ethyl 2-imidazolo[5,4-b]pyridin-2-ylacetate. As an alternate route, a substituted or unsubstituted ethyl 2-imidazolo[5,4-b]pyridin-2-ylacetate may be obtained from a compound such as the hydrochloride salt of 3-ethoxy-3-iminopropanoate and a substituted or unsubstituted 1,2-diaminopyridine. Reaction of a substituted or unsubstituted ethyl 2-imidazolo[5,4-b]pyridin-2-ylacetates with an aromatic compound having an amine and nitrile group such as substituted or unsubstituted 2-aminobenzonitrile with a base such as lithium bis(trimethylsilyl)amide provides the substituted or unsubstituted compound of structure II.

The instant invention also provides for compositions which may be prepared by mixing one or more compounds of the instant invention, or pharmaceutically acceptable salts or tautomers thereof, with pharmaceutically acceptable carriers, excipients, binders, diluents or the like, to treat or ameliorate a variety of disorders related to the activity of VEGF-RTK, more particularly angiogenesis associated with cancer. A therapeutically effective dose further refers to that amount of one or more compounds of the instant invention sufficient to result

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in amelioration of symptoms of the disorder. The pharmaceutical compositions of the instant invention can be manufactured by methods well known in the art such as conventional granulating, mixing, dissolving, encapsulating, lyophilizing, emulsifying or levigating processes, among others. The compositions can be in the form of, for example, granules, powders, tablets, capsules, syrup, suppositories, injections, emulsions, elixirs, suspensions or solutions. The instant compositions can be formulated for various routes of administration, for example, by oral administration, by transmucosal administration, by rectal administration, or subcutaneous administration as well as intrathecal, intravenous, intramuscular, intraperitoneal, intranasal, intraocular or intraventricular injection. The compound or compounds of the instant invention can also be administered in a local rather than a systemic fashion, such as injection as a sustained release formulation. The following dosage forms are given by way of example and should not be construed as limiting the instant invention.

For oral, buccal, and sublingual administration, powders, suspensions, granules, tablets, pills, capsules, gelcaps, and caplets are acceptable as solid dosage forms. These can be prepared, for example, by mixing one or more compounds of the instant invention, or pharmaceutically acceptable salts or tautomers thereof, with at least one additive or excipient such as a starch or other additive. Suitable additives or excipients are sucrose, lactose, cellulose sugar, mannitol, maltitol, dextran, sorbitol, starch, agar, alginates, chitins, chitosans, pectins, tragacanth gum, gum arabic, gelatins, collagens, casein, albumin, synthetic or semi-synthetic polymers or glycerides, methyl cellulose, hydroxypropylmethyl-cellulose, and/or polyvinylpyrrolidone. Optionally, oral dosage forms can contain other ingredients to aid in administration, such as an inactive diluent, or lubricants such as magnesium stearate, or preservatives such as paraben or sorbic acid, or anti-oxidants such as ascorbic acid, tocopherol or cysteine, a disintegrating agent, binders, thickeners, buffers, sweeteners, flavoring agents or perfuming agents. Additionally, dyestuffs or pigments may be added for identification. Tablets and pills may be further treated with suitable coating materials known in the art.

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Liquid dosage forms for oral administration may be in the form of pharmaceutically acceptable emulsions, syrups, elixirs, suspensions, slurries and solutions, which may contain an inactive diluent, such as water. Pharmaceutical formulations may be prepared as liquid suspensions or solutions using a sterile liquid, such as, but not limited to, an oil, water, an alcohol, and combinations of these. Pharmaceutically suitable surfactants, suspending agents, emulsifying agents, may be added for oral or parenteral administration.

As noted above, suspensions may include oils. Such oil include, but are not limited to, peanut oil, sesame oil, cottonseed oil, corn oil and olive oil. Suspension preparation may also contain esters of fatty acids such as ethyl oleate, isopropyl myristate, fatty acid glycerides and acetylated fatty acid glycerides. Suspension formulations may include alcohols, such as, but not limited to, ethanol, isopropyl alcohol, hexadecyl alcohol, glycerol and propylene glycol. Ethers, such as but not limited to, poly(ethyleneglycol), petroleum hydrocarbons such as mineral oil and petrolatum; and water may also be used in suspension formulations.

For nasal administration, the pharmaceutical formulations may be a spray or aerosol containing and appropriate solvents and optionally other compounds such as, but not limited to, stabilizers, antimicrobial agents, antioxidants, pH modifiers, surfactants, bioavailability modifiers and combinations of these. A propellant for an aerosol formulation may include compressed air, nitrogen, carbon dioxide, or a hydrocarbon based low boiling solvent. The compound or compounds of the instant invention are conveniently delivered in the form of an aerosol spray presentation from a nebulizer or the like.

Injectable dosage forms generally include aqueous suspensions or oil suspensions which may be prepared using a suitable dispersant or wetting agent and a suspending agent. Injectable forms may be in solution phase or in the form of a suspension, which is prepared with a solvent or diluent. Acceptable solvents or vehicles include sterilized water, Ringer's solution, or an isotonic aqueous saline solution. Alternatively, sterile oils may be employed as solvents or suspending

agents. Preferably, the oil or fatty acid is non-volatile, including natural or synthetic oils, fatty acids, mono-, di- or tri-glycerides.

For injection, the pharmaceutical formulation may be a powder suitable for reconstitution with an appropriate solution as described above.

- 5 Examples of these include, but are not limited to, freeze dried, rotary dried or spray dried powders, amorphous powders, granules, precipitates, or particulates. For injection, the formulations may optionally contain stabilizers, pH modifiers, surfactants, bioavailability modifiers and combinations of these. The compounds may be formulated for parenteral administration by injection such as by bolus
- 10 injection or continuous infusion. A unit dosage form for injection may be in ampoules or in multi-dose containers.

- For rectal administration, the pharmaceutical formulations may be in the form of a suppository, an ointment, an enema, a tablet or a cream for release of compound in the intestines, sigmoid flexure and/or rectum. Rectal suppositories are
- 15 prepared by mixing one or more compounds of the instant invention, or pharmaceutically acceptable salts or tautomers of the compound, with acceptable vehicles, for example, cocoa butter or polyethylene glycol, which is present in a solid phase at normal storing temperatures, and present in a liquid phase at those temperatures suitable to release a drug inside the body, such as in the rectum. Oils
- 20 may also be employed in the preparation of formulations of the soft gelatin type and suppositories. Water, saline, aqueous dextrose and related sugar solutions, and glycerols may be employed in the preparation of suspension formulations which may also contain suspending agents such as pectins, carbomers, methyl cellulose, hydroxypropyl cellulose or carboxymethyl cellulose, as well as buffers and
- 25 preservatives.

Besides those representative dosage forms described above, pharmaceutically acceptable excipients and carries are generally known to those skilled in the art and are thus included in the instant invention. Such excipients and

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carriers are described, for example, in "Remingtons Pharmaceutical Sciences" Mack Pub. Co., New Jersey (1991), which is incorporated herein by reference.

The formulations of the invention may be designed for to be short-acting, fast-releasing, long-acting, and sustained-releasing as described below.

- 5 Thus, the pharmaceutical formulations may also be formulated for controlled release or for slow release.

- The instant compositions may also comprise, for example, micelles or liposomes, or some other encapsulated form, or may be administered in an extended release form to provide a prolonged storage and/or delivery effect. Therefore, the  
10 pharmaceutical formulations may be compressed into pellets or cylinders and implanted intramuscularly or subcutaneously as depot injections or as implants such as stents. Such implants may employ known inert materials such as silicones and biodegradable polymers.

- Specific dosages may be adjusted depending on conditions of disease,  
15 the age, body weight, general health conditions, sex, and diet of the subject, dose intervals, administration routes, excretion rate, and combinations of drugs. Any of the above dosage forms containing effective amounts are well within the bounds of routine experimentation and therefore, well within the scope of the instant invention.

- A therapeutically effective dose may vary depending upon the route  
20 of administration and dosage form. The preferred compound or compounds of the instant invention is a formulation that exhibits a high therapeutic index. The therapeutic index is the dose ratio between toxic and therapeutic effects which can be expressed as the ratio between  $LD_{50}$  and  $ED_{50}$ . The  $LD_{50}$  is the dose lethal to 50% of the population and the  $ED_{50}$  is the dose therapeutically effective in 50% of  
25 the population. The  $LD_{50}$  and  $ED_{50}$  are determined by standard pharmaceutical procedures in animal cell cultures or experimental animals.

"Treating" within the context of the instant invention, means an alleviation of symptoms associated with a disorder or disease, or halt of further

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- progression or worsening of those symptoms, or prevention or prophylaxis of the disease or disorder. For example, within the context of treating patients in need of an inhibitor of VEGF-RTK, successful treatment may include a reduction in the proliferation of capillaries feeding a tumor or diseased tissue, an alleviation of
- 5 symptoms related to a cancerous growth or tumor, proliferation of capillaries, or diseased tissue, a halting in capillary proliferation, or a halting in the progression of a disease such as cancer or in the growth of cancerous cells. Treatment may also include administering the pharmaceutical formulations of the present invention in combination with other therapies. For example, the compounds and pharmaceutical
- 10 formulations of the present invention may be administered before, during, or after surgical procedure and/or radiation therapy. The compounds of the invention can also be administered in conjunction with other anti-cancer drugs including those used in antisense and gene therapy. For example, the compounds of the invention can be administered in conjunction with anti-cancer drugs such as 5-FU and/or CPT-11.
- 15 Synergistic effects were observed when 5-FU and/or CPT-11 were administered along with compounds of the present invention such as 4-amino-3-{5-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one.

- A method of treating a patient in need of an inhibitor of vascular endothelial growth factor receptor tyrosine kinase includes administering an
- 20 effective amount of a pharmaceutical formulation according to the invention to a patient in need thereof.

A method for inhibiting tumor growth in a patient includes administering an effective amount of the compound or a pharmaceutically acceptable salt thereof to a patient having a tumor.

- 25 A method for inhibiting the proliferation of capillaries in a patient includes administering an effective amount of the compound or a pharmaceutically acceptable salt thereof according to a patient in need.

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A method of preparing pharmaceutical formulations includes mixing any of the above-described compounds with a pharmaceutically acceptable carrier and water or an aqueous solution.

The present invention, thus generally described, will be understood more readily by reference to the following examples, which are provided by way of illustration and are not intended to be limiting of the present invention.

### EXAMPLES

The following abbreviations are used in the Examples:

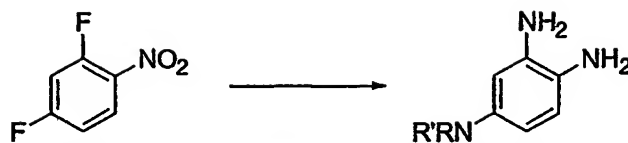
	ATP:	Adenosine triphosphate
10	BSA:	Bovine Serum Albumin
	DMA:	<i>N,N</i> -Dimethylacetamide
	DMF:	<i>N,N</i> -Dimethylformamide
	dppf:	1,1'-(diphenylphosphino)ferrocene
	DTT:	DL-Dithiothreitol
15	EDTA:	Ethylene diamine tetraacetic acid
	EtOAc:	Ethyl acetate
	EtOH:	Ethanol
	HBTU:	O-Benzotriazol-1-yl- <i>N,N,N',N'</i> -tetramethyluronium hexafluorophosphate
20	IC <sub>50</sub> value:	The concentration of an inhibitor that causes a 50 % reduction in a measured activity.
	LiHMDS:	Lithium bis(trimethylsilyl)amide
	MeOH:	Methanol
	NMP:	<i>N</i> -methylpyrrolidone
25	THF:	Tetrahydrofuran

The compounds were named using Nomenclator (v. 3.0 & v. 5.0) from CmemInovation Software, Inc. and ACD/Name v. 4.53.

The various aryl diamine starting materials used to synthesize benzimidazole acetates may be obtained from commercial sources, prepared by methods known to one of skill in the art, or prepared by the following general Methods 1-15.



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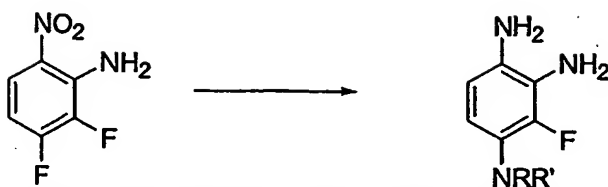
**Method 1**

- 2,4-Difluoronitrobenzene (1.0 eq) was placed in a dry round-bottomed flask equipped with a dry ice condenser charged with acetone and dry ice.
- 5 Ammonia was condensed into the flask and the resulting solution was stirred at reflux for 7 hours. A yellow precipitate formed within 1 hour. After 7 hours, the condenser was removed and the liquid ammonia was allowed to evaporate over several hours. The crude product was purified by flash chromatography on silica gel (85:15 hexanes:ethyl acetate, product at  $R_f = 0.32$ , contaminant at  $R_f = 0.51$ );
- 10 GC/MS  $m/z$  156.1 ( $M^+$ ),  $R_t$  11.16 minutes.

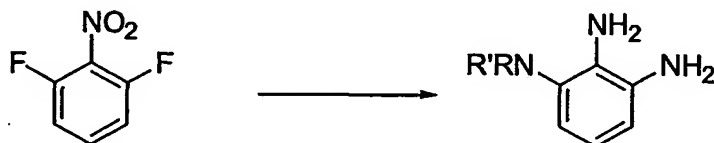
- The resulting 5-fluoro-2-nitrophenylamine (1.0 eq) and an amine (1.1 eq) e.g. N-methyl piperazine, were dissolved in NMP and triethylamine (2.0 eq) was added. The reaction mixture was heated at 100°C for 3 hours. The solution was then cooled to room temperature and diluted with water. The resulting
- 15 precipitate was filtered and dried under vacuum to provide the 2-nitro-diamino product. Alternatively, the same product may be obtained from commercially available 5-chloro-2-nitrophenylamine under identical conditions except heating at 130°C for 1-2 days. In some examples, the displacement on either 5-fluoro-2-nitrophenylamine or 5-chloro-2-nitrophenylamine can be conducted in neat amine (5
- 20 eq) at 100°C or 130 °C, respectively. The product is isolated in an identical manner. LC/MS  $m/z$  237.1 ( $MH^+$ ),  $R_t$  1.304 minutes.

- The nitroamine (1.0 eq) and 10% Pd/C (0.1 eq) was suspended in anhydrous ethanol at room temperature. The reaction flask was evacuated and subsequently filled with  $H_2$ . The resulting mixture was then stirred under a
- 25 hydrogen atmosphere overnight. The resulting solution was filtered through Celite and concentrated under vacuum to provide the crude product which was used without further purification.

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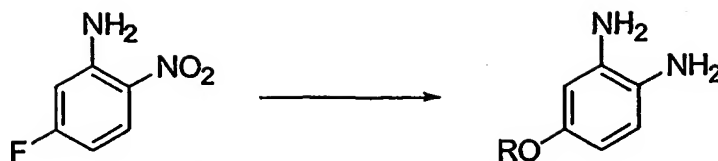
**Method 2**

A round-bottom flask was charged with 2,3-difluoro-6-nitrophenylamine (1 eq) and enough NMP to make a viscous slurry. An amine (5 eq), e.g. N-methyl piperazine, was added and the solution was heated at 100°C. After 2 hours, the solution was cooled and poured into water. A bright yellow solid formed which was filtered and dried. The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification. LC/MS  $m/z$  225.1 (MH<sup>+</sup>), R<sub>t</sub> 0.335 minutes.

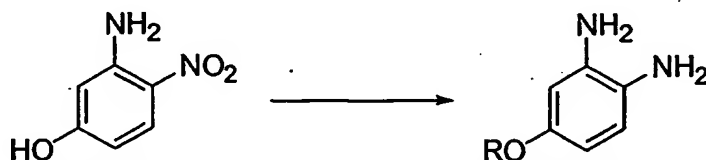
10 **Method 3**

To a 0.1 M DMF solution of 1,3-difluoro-2-nitrobenzene was added Et<sub>3</sub>N (2 eq) followed by an amine (1 eq), e.g. morpholine. The mixture was stirred for 18 hours and then diluted with water and extracted with ethyl acetate. LC/MS  $m/z$  227.2 (MH<sup>+</sup>), R<sub>t</sub> 2.522 minutes. The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Ammonia was condensed into a bomb containing the crude product. The bomb was sealed and heated to 100°C (over 400 psi). After 72 hours the bomb was allowed to cool and the ammonia was evaporated to provide a reddish solid. The nitroamine was reduced as in Method 1 to provide the crude product which was used without further purification. LC/MS  $m/z$  194.1 (MH<sup>+</sup>), R<sub>t</sub> 1.199 minutes.

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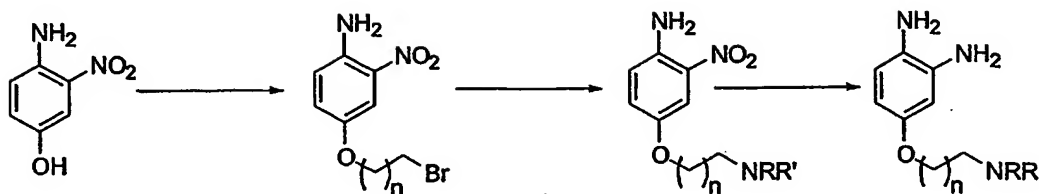
**Method 4**

To a stirred NMP solution containing NaH (1.3 eq) was added an alcohol (1.0 eq), e.g. 2-methoxyethanol. The resulting mixture was then stirred  
5 for 30 minutes. A slurry of 5-fluoro-2-nitrophenylamine in NMP was then added slowly. The mixture was then heated to 100°C. After 2 hours, the reaction mixture was cooled and water was added. The mixture was then filtered and the captured solid was washed with water and purified by silica gel chromatography (1:1 ethyl acetate:hexane). LC/MS *m/z* 213.2 (MH<sup>+</sup>), R 2.24 minutes. The nitroamine was  
10 reduced as in Method 1 to provide the crude product which was used without further purification. LC/MS *m/z* 183.1 (MH<sup>+</sup>), R 0.984 minutes.

**Method 5**

Diisopropyl azodicarboxylate (1.1 eq) was added dropwise to a  
15 stirred solution of 4-amino-3-nitrophenol (1.0 eq), triphenylphosphine (1.1 eq), and an alcohol, e.g. N-(2-hydroxyethyl)morpholine (1.0 eq), in tetrahydrofuran at 0°C. The mixture was allowed to warm to room temperature and stirred for 18 hours. The solvent was evaporated, and the product was purified by silica gel chromatography (98:2 CH<sub>2</sub>Cl<sub>2</sub>:methanol) to yield 4-(2-morpholin-4-ylethoxy)-2-  
20 nitrophenylamine as a dark reddish-brown oil. LC/MS *m/z* 268.0 (MH<sup>+</sup>), R 1.01 minutes. The nitroamine was reduced as in Method 1 to give the crude product which was used without further purification. LC/MS *m/z* 238.3 (MH<sup>+</sup>), R 0.295 minutes.

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**Method 6**

To a flask charged with 4-amino-3-nitrophenol (1 eq),  $\text{K}_2\text{CO}_3$  (2 eq),  
 5 and 2-butanone was added an alkyl dibromide, e.g. 1,3-dibromopropane  
 (1.5 eq). The resulting mixture was then heated at  $80^\circ\text{C}$  for 18 hours. After  
 cooling, the mixture was filtered, concentrated, and diluted with water. The  
 solution was then extracted with  $\text{CH}_2\text{Cl}_2$  (3 x) and the combined organic layers were  
 concentrated to give a solid that was then washed with pentane. LCMS  $m/z$  275.1  
 10 (MH<sup>+</sup>), R<sub>t</sub> 2.74 minutes.

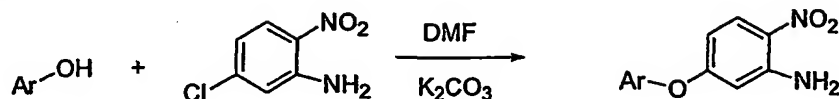
An acetonitrile solution of the bromide prepared above, an amine,  
 e.g. pyrrolidine (5 eq),  $\text{Cs}_2\text{CO}_3$  (2 eq) and  $\text{Bu}_4\text{NI}$  (0.1 eq) was heated at  $70^\circ\text{C}$  for 48  
 hours. The reaction mixture was cooled, filtered, and concentrated. The residue  
 was dissolved in  $\text{CH}_2\text{Cl}_2$ , washed with water, and concentrated to give the desired  
 15 nitroamine, 2-nitro-4-(3-pyrrolidin-1-ylpropoxy)phenylamine. LCMS  $m/z$  266.2  
 (MH<sup>+</sup>), R<sub>t</sub> 1.51 minutes. The nitroamine was reduced as in Method 1 to provide  
 the crude product which was used without further purification.

**Method 7**

20 To a suspension of 6-chloro-3-nitropyridin-2-amine (1 eq) in  
 acetonitrile was added an amine, e.g. morpholine (4 eq). The resulting reaction  
 mixture was stirred at  $70^\circ\text{C}$  for 5 hours. The solvent was evaporated under reduced  
 pressure, and the residue triturated with ether to provide the desired compound as a  
 bright yellow powder. LC/MS  $m/z$  225.0 (MH<sup>+</sup>), R<sub>t</sub> 1.79 minutes. The nitroamine

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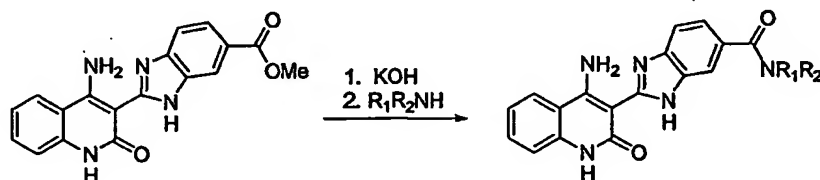
was reduced as in Method 1 to provide the crude product which was used without further purification.

**Method 8:**

5

A phenol (1 equivalent) and 5-chloro-2-nitro aniline (1 equivalent) were dissolved in DMF, and solid K<sub>2</sub>CO<sub>3</sub> (2 equivalents) was added in one portion. The reaction mixture was heated at 120°C overnight. The reaction mixture was cooled to room temperature, most of the DMF was distilled off, and water was added to the residue to obtain a precipitate. The solid was dried and purified by chromatography on silicagel (2-10% MeOH/CH<sub>2</sub>Cl<sub>2</sub>) to afford the desired product. The nitroamine was reduced as in method 1 to give the crude product that was used without further purification.

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**Method 9**

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Furthermore, the introduction of substituents on the benzimidazole ring need not be limited to the early stages of the synthesis and may arise after formation of the quinolinone ring. For example, the crude methyl ester shown in the figure above was dissolved in a 1:1 mixture of EtOH and 30% aqueous KOH and stirred overnight at 70°C. The reaction mixture was then cooled and acidified with 1N HCl to give a precipitate. The solid was filtered, washed with water and dried to obtain 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazole-6-carboxylic acid 2-(4-amino-2-oxo-3-hydroquinolyl)benzimidazole-6-carboxylic acid as a brown solid. LC/MS *m/z*: 321.1 (MH<sup>+</sup>), R 2.26 minutes.

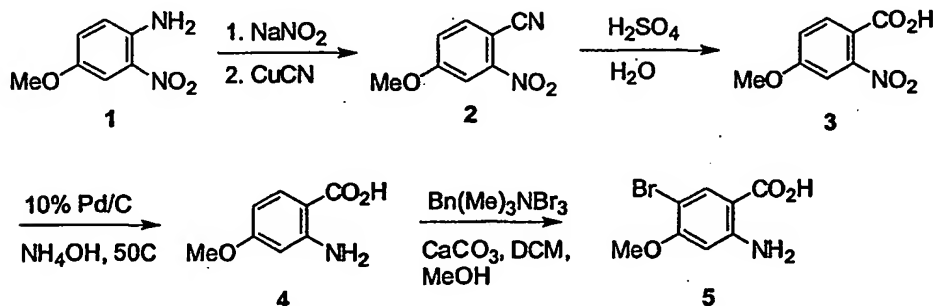
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A mixture of 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazole-6-carboxylic acid (1 eq) the amine (1 eq), EDC (1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 1.2 eq), HOAT (1-hydroxy-7-azabenzotriazole, 1.2 eq) and triethylamine (2.5 eq) in DMF, was stirred at 23 °C for 20 h. The reaction mixture was partitioned between water and ethyl acetate. The combined organic layers were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated. Water was added and the precipitate thus formed was filtered off and dried to afford the desired product.

The various 2-amino benzoic acid starting materials used to synthesize isatoic anhydrides may be obtained from commercial sources, prepared by methods known to one of skill in the art, or prepared by the following general Methods 10-11. General isatoic anhydride synthesis methods are described in *J. Med. Chem.* 1981, 24 (6), 735 and *J. Heterocycl. Chem.* 1975, 12(3), 565.

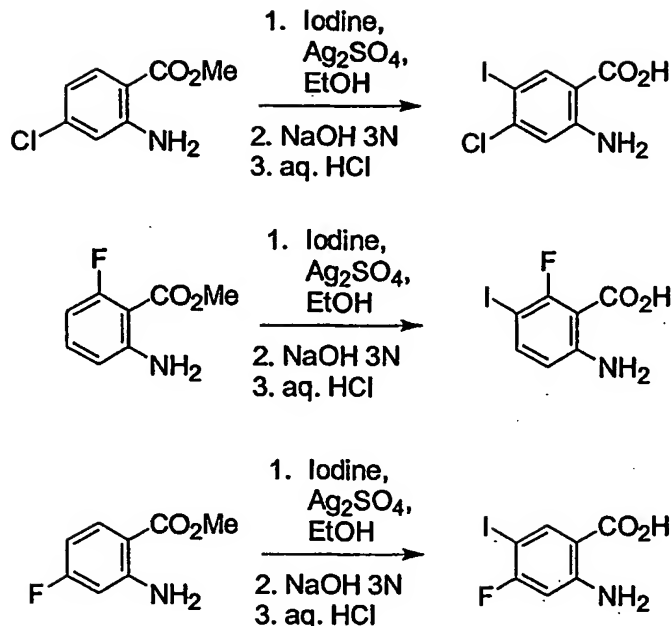
**Method 10**

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Compounds 1-3 were made using similar procedures as found in U.S. Patent No. 4,287,341. Compound 3 was reduced using standard hydrogenation conditions of 10% Pd/C in NH<sub>4</sub>OH at 50°C over 48 hours. The product was precipitated by neutralizing with glacial acetic acid, filtering, and washing with water and ether. Yields were about 50%. Compound 5 was prepared in a manner similar to that disclosed in U.S. Patent No. 5,716,993.

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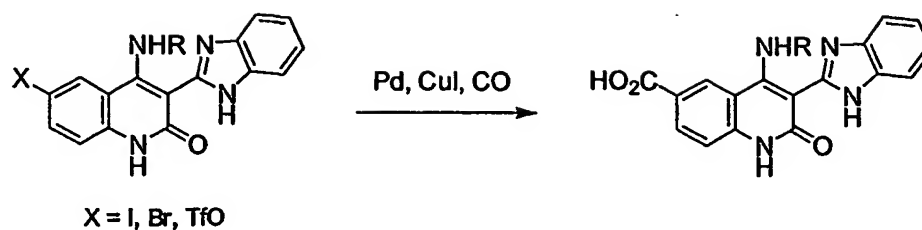
## Method 11



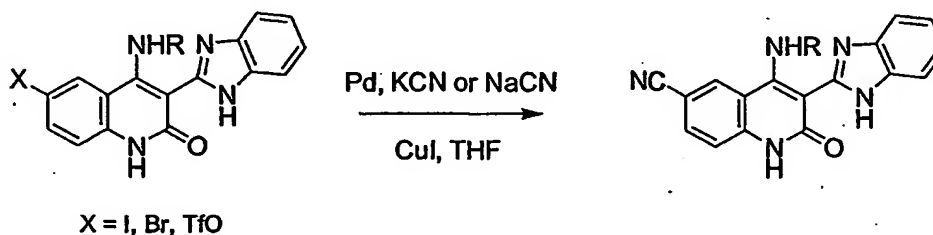
- Iodination of aniline containing compounds: Iodination was done by a similar procedure as in *J. Med. Chem.* 2001, 44, 6, 917-922. The anthranilic ester in EtOH was added to a mixture of silver sulfate (1 equivalent) and I<sub>2</sub> (1 equivalent). The reaction was typically done after 3 hours at room temperature. The reaction was filtered through celite and concentrated. The residue was taken up in EtOAc and washed with aqueous saturated NaHCO<sub>3</sub> (3x), water (3x), brine (1x), dried (MgSO<sub>4</sub>), filtered, and concentrated. The crude product (~5 g) was dissolved in MeOH (60-100 ml), NaOH 6N (25 ml), and water (250 ml). The reactions were typically done after heating at 70-80°C for 4 hours. The reaction mixture was extracted with EtOAc (2x), neutralized with aqueous HCl, filtered to collect the solids, and the solid products were washed with water. The products were dried in vacuo.

In various instances, substitutions on the quinolinone ring may also be introduced after coupling as shown in the general methods 12-15.

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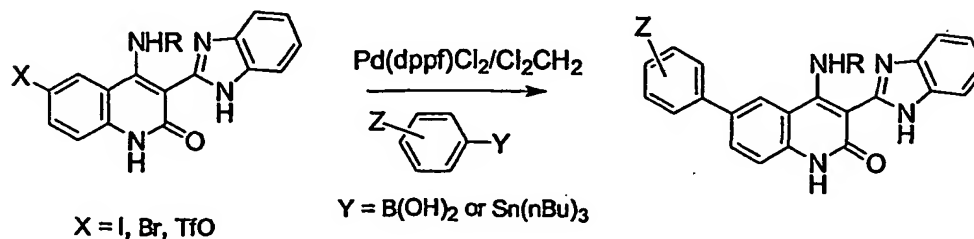
**Method 12**

Conversion of the C-6 or C-7 halides to an acid group was accomplished using procedures in the following references - Koga, H.; et al., *Tet. Let.*, 1995, 36, 1, 87-90 and Fukuyama, T.; et al., *J. Am. Chem. Soc.*, 1994, 116, 3125-3126.

**Method 13**

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Conversion of the C-6 or C-7 halides to a cyano group was accomplished using procedures in the following reference - Anderson, B.A.; et al., *J. Org. Chem.*, 1998, 63, 8224-828.

**Method 14**

15

Conversion of the C-6 or C-7 halides to an aryl group was accomplished using standard Suzuki or Stille procedures such as described below.

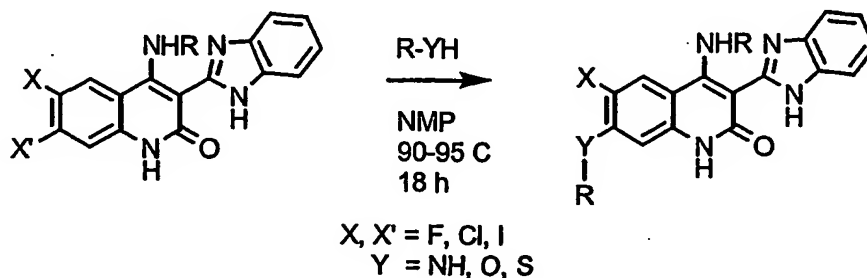


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Suzuki Method: To a 1 dram (4 ml) vial was added sequentially the quinolone (1 equivalent), boronic acid (1.2-1.5 equivalents), Pd(dppf)Cl<sub>2</sub>, Cl<sub>2</sub>CH<sub>2</sub> (0.2 equivalents), DMF (0.5 - 1 ml) and TEA (4 equivalents). The reaction was flushed with argon, capped and heated at 85°C for 12 hours. Once done, the reaction is cooled to room temperature, and filtered with a syringe filter disk. The clear solution is then neutralized with TFA (a couple of drops) and injected directly onto a preparative HPLC. The products are lyophilized to dryness.

Stille Method: To a 1 dram (4 ml) vial was added sequentially the quinolone (1 equivalent), tin reagent (1.8 equivalent), Pd(dppf)Cl<sub>2</sub> · Cl<sub>2</sub>CH<sub>2</sub> (0.2 equivalents), and DMF (0.5 - 1 ml). The reaction was flushed with argon, capped and heated at 60-85°C for 4 hours. Once done, the reaction is cooled to room temperature, and filtered with a syringe filter disk. The clear solution is then neutralized with TFA (a couple of drops) and injected directly onto a preparative HPLC. The products are lyophilized to dryness.

#### 15 Method 15



A dihaloquinolone such as a difluoroquinolone (12-15 mg) was placed in a 1 dram (2 ml) vial. NMP (dry and pre-purged with argon for 5 minutes) was added to the vial (0.5 ml). The amine reagent (40-50 mg) was added next. If the amine was an HCl salt, the reaction was neutralized with TEA (~1.2-1.5 equivalents). The reaction was purged again with argon for about 5 seconds, and immediately capped. The reaction was typically heated in a heating block at 90-95°C for 18 hours. The reaction was followed by HPLC or LCMS. After taking samples for HPLC, the vial was purged with argon again and capped. Some

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coupling partners took 24 or 48 hours to reach completion. Less nucleophilic amines like pyrrole required the addition of a strong base to reach completion. In these cases, cesium carbonate (2 equivalents based on the amine used) was added to the reaction. Once done, the reaction was cooled to room temperature, and filtered with a syringe filter disk. The clear solution was then neutralized with TFA (a couple of drops) and injected directly onto a preparative HPLC. The products were lyophilized to dryness.

### Example 1

#### **Ethyl 2-benzimidazol-2-ylacetate**

10                   A solution of 1,2-phenylenediamine (1.0 eq) and ethyl 3-ethoxy-3-  
iminopropanoate hydrochloride (1.3 eq) in ethanol was stirred at 90°C overnight.  
The reaction was cooled to room temperature and the solvent was removed *in vacuo*. Water and CH<sub>2</sub>Cl<sub>2</sub> were added to the residue. The organic layer was separated, dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent removed. The solid recovered was  
15                   used without purification. LC/MS *m/z* 205.2 (MH<sup>+</sup>), R<sub>t</sub> 1.44 minutes.

#### **5-(4-Methylpiperazinyl)-2-nitrobenzenecarbonitrile**

5-Fluoro-2-nitrobenzenecarbonitrile (1.02 eq) and N-methylpiperazine (1.0 eq) were dissolved in NMP. Triethylamine (2.1 eq) was added, and the resulting solution heated at 100°C for 1 hour. The solution was  
20                   cooled to room temperature and poured into H<sub>2</sub>O. A precipitate formed which was filtered to yield the desired product as a green solid. LC/MS *m/z* 247.3 (MH<sup>+</sup>), R<sub>t</sub> 1.46 minutes.

#### **2-Amino-5-(4-methylpiperazinyl)benzenecarbonitrile**

5-(4-Methylpiperazinyl)-2-nitrobenzenecarbonitrile (1.0 eq) was  
25                   dissolved in EtOAc. The flask was purged with nitrogen, and 10% Pd/C (0.1 eq) was added. The flask was evacuated and purged with H<sub>2</sub> three times. The resulting mixture was stirred for three days at room temperature. The mixture was filtered through Celite and the filter pad was washed with EtOAc. The solvent was

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removed *in vacuo* to give a yellow solid which was purified by silica gel chromatography (5:1:95 MeOH:Et<sub>3</sub>N:EtOAc) to give the desired product as a yellow solid. LC/MS *m/z* 217.3 (MH<sup>+</sup>), R<sub>t</sub> 0.95 minutes.

#### Method A

- 5    **4-Amino-3-benzimidazol-2-yl-6-(4-methylpiperazinyl)hydroquinolin-2-one**  
Ethyl 2-benzimidazol-2-ylacetate (1.1 eq) and 2-amino-5-(4-methylpiperazinyl)benzenecarbonitrile (1.0 eq) were dissolved in 1,2-dichloroethane, and then SnCl<sub>4</sub> (11 eq) was added. The mixture was heated at reflux overnight. Upon cooling, the mixture was concentrated *in vacuo*. NaOH (3  
10    M) was added to the solid, and the mixture heated at 80°C for 0.5 hours. The solid was filtered and washed sequentially with H<sub>2</sub>O, CH<sub>2</sub>Cl<sub>2</sub>, and acetone. LC/MS indicated that the product was present in the acetone layer and the solid. These fractions were combined and purified by silica gel chromatography (5-10% MeOH in CH<sub>2</sub>Cl<sub>2</sub> with 1% Et<sub>3</sub>N) to give the desired product. LC/MS *m/z* 375.4 (MH<sup>+</sup>),  
15    R<sub>t</sub> 1.65 minutes.

#### Example 2

##### **6-Amino-2-(2-morpholin-4-ylethoxy)benzenecarbonitrile**

- 4-(Hydroxyethyl)morpholine (1.02 eq) was added to NaH (1.2 eq) in NMP. After 10 minutes, 6-amino-2-fluorobenzenecarbonitrile (1.0 eq) was added  
20    in NMP. The resulting mixture was heated at 100°C for 1 hour. The mixture was then cooled and poured into H<sub>2</sub>O. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated *in vacuo* to yield a brown gum. The crude material was purified by silica gel chromatography (5:1:95 MeOH:Et<sub>3</sub>N:EtOAc) to give the desired  
25    product. LC/MS *m/z* 248.3 (MH<sup>+</sup>), R<sub>t</sub> 1.26 minutes.

**4-Amino-3-benzimidazol-2-yl-5-(2-morpholin-4-ylethoxy)hydroquinolin-2-one**  
The title compound was synthesized as described in Example 1, Method A using

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6-amino-2-(2-morpholin-4-ylethoxy)benzenecarbonitrile. LC/MS  $m/z$  406.4 (MH<sup>+</sup>), R<sub>t</sub> 1.67 minutes.

### Example 3

#### **4-(2-Morpholin-4-ylethoxy)-2-nitrophenylamine**

5 Diisopropyl azodicarboxylate (1.1 eq) was added dropwise to a stirred solution of 4-amino-3-nitrophenol (1.0 eq), triphenylphosphine (1.1 eq), and N-(2-hydroxyethyl)morpholine (1.0 eq), in THF at 0°C. The mixture was allowed to warm to room temperature and left to stir for 18 hours. The solvent was evaporated and the product was purified by silica gel chromatography (98:2  
10 CH<sub>2</sub>Cl<sub>2</sub>:MeOH) to yield a dark reddish-brown oil. LC/MS  $m/z$  268.0 (MH<sup>+</sup>), R<sub>t</sub> 1.01 minutes.

#### **4-(2-Morpholin-4-ylethoxy)benzene-1,2-diamine**

To a solution 4-(2-morpholin-4-ylethoxy)-2-nitrophenylamine (1.0 eq) in EtOH was added Pd/C (0.1 eq). The reaction vessel was repeatedly purged with  
15 nitrogen, then stirred under a hydrogen atmosphere (1 atm) for 18 hours. The product was filtered through a Celite plug, and the plug washed with EtOH. The diamine was used without purification. LC/MS  $m/z$  238.3 (MH<sup>+</sup>), R<sub>t</sub> 0.295 minutes.

#### **Ethyl 2-[5-(2-morpholin-4-ylethoxy)benzimidazol-2-yl]acetate**

20 The title compound was synthesized as described in Example 1 using 4-(2-morpholin-4-ylethoxy)benzene-1,2-diamine. The organic layer was concentrated and the residue was purified by silica gel chromatography (10:1:2 CH<sub>2</sub>Cl<sub>2</sub>:MeOH:EtOAc) to yield a dark reddish brown oil. LC/MS  $m/z$  334.4 (MH<sup>+</sup>) R<sub>t</sub> 1.08 minutes.

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**4-Amino-3-[5-(2-morpholin-4-ylethoxy)benzimidazol-2-yl]-6-nitrohydroquinolin-2-one**

The title compound was synthesized as described in Example 1, Method A using ethyl 2-[5-(2-morpholin-4-ylethoxy)benzimidazol-2-yl]acetate and 5-nitroanthranilonitrile. The crude product was purified by silica gel chromatography (5-10% MeOH in CH<sub>2</sub>Cl<sub>2</sub> with 1% Et<sub>3</sub>N) to give the desired product. LC/MS *m/z* 451.2 (MH<sup>+</sup>), R<sub>t</sub> 1.89 minutes.

**Example 4****10 4-Amino-5-(2-morpholin-4-ylethoxy)-3-[5-(2-morpholin-4-ylethoxy)-benzimidazol-2-yl]hydroquinolin-2-one**

The title compound was synthesized as described in Example 1, Method A using ethyl 2-[5-(2-morpholin-4-ylethoxy)benzimidazol-2-yl]acetate and 6-amino-2-(2-morpholin-4-ylethoxy)benzenecarbonitrile. LC/MS *m/z* 535.4 (MH<sup>+</sup>), R<sub>t</sub> 1.44 minutes.

**15 Example 5****2-[(Ethoxycarbonyl)methyl]benzimidazole-5-carboxylic acid**

The title compound was synthesized as described in Example 1 using 3,4-diaminobenzoic acid. The crude material was purified by silica gel chromatography (5:95 MeOH:CH<sub>2</sub>Cl<sub>2</sub>) to afford the desired product as a white to off-white solid. LC/MS *m/z* 249.1 (MH<sup>+</sup>), R<sub>t</sub> 1.35 minutes.

**Ethyl 2-[5-(N,N-dimethylcarbamoyl)benzimidazol-2-yl]acetate**

2-[(Ethoxycarbonyl)methyl]benzimidazole-5-carboxylic acid (1.0 eq) was dissolved in THF. HBTU (1.1 eq) and diisopropylethylamine (2.0 eq) were added, followed by dimethylamine (2.0 M in THF, 1.1 eq). The reaction was stirred at room temperature overnight then concentrated and the resulting residue was purified by silica gel chromatography (5:95 MeOH:CH<sub>2</sub>Cl<sub>2</sub>) to afford the desired compound. LC/MS *m/z* 276.2 (MH<sup>+</sup>), R<sub>t</sub> 1.18 minutes.

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**[2-(4-amino-2-oxo(3-hydroquinolyl))benzimidazol-5-yl]-N,N-dimethylcarboxamide.**

The title compound was synthesized as described in Example 1, Method A using ethyl 2-[5-(N,N-dimethylcarbamoyl)benzimidazol-2-yl]acetate and anthranilonitrile. The resulting solid was collected by filtration and washed with water followed by acetone to afford the desired product as a white solid. LC/MS *m/z* 348.3 (MH<sup>+</sup>), *R<sub>t</sub>* 1.87 minutes.

**Example 6**

**4-Amino-3-[5-(morpholin-4-ylcarbonyl)benzimidazol-2-yl]hydroquinolin-2-one.**

2-[(Ethoxycarbonyl)methyl]benzimidazole-5-carboxylic acid (1.0 eq) was dissolved in THF. HBTU (1.1 eq) and diisopropylethylamine (2.0 eq) were added, followed by morpholine (1.1 eq). The reaction was stirred at room temperature for 3 days then concentrated and purified by silica gel chromatography (5-10% methanol/dichloromethane). The product-containing fractions were concentrated and dissolved in anhydrous 1,2-dichloroethane. Anthranilonitrile (1.0 eq) was added followed by SnCl<sub>4</sub> (5.0 eq) and the reaction was heated at 90°C overnight. The reaction mixture was concentrated and the resulting residue was redissolved in NaOH (2 M) and heated at 90°C for 4 hours. After cooling to room temperature, the resulting solid was collected and washed with water followed by acetone to afford the desired product. LC/MS *m/z* 390.2 (MH<sup>+</sup>), *R<sub>t</sub>* 1.95 minutes.

**Example 7**

**4-Bromobenzene-1,2-diamine**

A solution of 4-bromo-2-nitroaniline (1.0 eq) and SnCl<sub>2</sub> (2.2 eq) in EtOH was heated at reflux for 3 hours. After this time, the solution was poured onto ice, brought to pH 10 with 2M NaOH and extracted with Et<sub>2</sub>O. The combined organic layers were dried over MgSO<sub>4</sub> and concentrated. The resulting brown oil was purified by silica gel chromatography (0-50% EtOAc:hexanes) to provide a light yellow solid. LC/MS *m/z* 187.1 (MH<sup>+</sup>), *R<sub>t</sub>* 1.33 minutes.

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**2-Nitro-4-(2-thienyl)phenylamine**

4-Bromo-2-nitroaniline (1.0 eq) and  $\text{Na}_2\text{CO}_3$  (2.0 eq) were dissolved in DMF/ $\text{H}_2\text{O}$  (5:1) at room temperature. Nitrogen was bubbled through the reaction mixture for 5 minutes and  $\text{PdCl}_2(\text{dppf})_2$  (0.1 eq) was added. After stirring at 23°C for approximately 10 minutes, 2-thiopeneboronic acid (1.1 eq) in DMF was added and the reaction was heated at 90°C for 12 hours. After this time, the solution was concentrated and partitioned between EtOAc and  $\text{H}_2\text{O}$ . The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. The resulting black residue was purified by silica gel chromatography (0-20% EtOAc:hexanes) to yield an orange solid. LC/MS  $m/z$  221.1 ( $\text{MH}^+$ ), R<sub>t</sub> 2.67 minutes.

**Ethyl 2-[5-(2-thienyl)benzimidazol-2-yl]acetate**

2-Nitro-4-(2-thienyl)phenylamine (1.0 eq) and 10% Pd/C (0.1 eq) were suspended in anhydrous EtOH at room temperature. The reaction flask was evacuated and subsequently filled with  $\text{H}_2$ . The resulting mixture was allowed to stir under a hydrogen atmosphere for 3 hours. Ethyl 3-ethoxy-3-iminopropanoate hydrochloride (2.0 eq) was then added and the resulting mixture was heated at reflux for 12 hours. After this time, the solution was filtered through a plug of Celite, concentrated, dissolved in 50 ml of 2N HCl and washed with  $\text{CH}_2\text{Cl}_2$ . The aqueous layer was brought to pH 12 with concentrated  $\text{NH}_4\text{OH}(\text{aq})$  and extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were dried with  $\text{MgSO}_4$  and concentrated to yield a brown oil which was purified by silica gel chromatography (5:95 MeOH: $\text{CH}_2\text{Cl}_2$ ) to provide a yellow solid. LC/MS  $m/z$  287.1 ( $\text{MH}^+$ ), R<sub>t</sub> 1.98 minutes.

**4-Amino-3-[5-(2-thienyl)benzimidazol-2-yl]hydroquinolin-2-one**

The title compound was synthesized as described in Example 1, Method A using ethyl 2-[5-(2-thienyl)benzimidazol-2-yl]acetate and anthranilonitrile. LC/MS  $m/z$  359.2 ( $\text{MH}^+$ ), R<sub>t</sub> 2.68 minutes.

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**Example 8****5-Fluoro-2-nitrophenylamine**

2,4-Difluoronitrobenzene (1.0 eq) was placed in a dry round-bottomed flask equipped with a dry ice condenser charged with acetone/dry ice.

- 5 Ammonia was condensed into the flask and the resulting solution was stirred at reflux for 7 hours. A yellow precipitate was formed within 1 hours. After 7 hours, the condenser was removed and the liquid ammonia was allowed to evaporate over several hours. The crude product was purified by flash chromatography on silica gel (85:15 hexanes:EtOAc, product at  $R_f = 0.32$ , contaminant at  $R_f = 0.51$ ).

- 10 GC/MS  $m/z$  156.1 (M+),  $R_t$  11.16 minutes.

**2-Nitro-5-[1-(1,2,4-triazolyl)]phenylamine**

5-Fluoro-2-nitrophenylamine (1.0 eq), 1H-1,2,4-triazole (3.0 eq) and NaH (3.0 eq) in NMP were heated at 100°C for 1 hour. The solution was cooled to room temperature and slowly poured onto ice water. The resulting precipitate was

15 filtered and dried under vacuum to yield the desired product. The resulting solid was recrystallized from EtOH to afford pure product as a bright yellow solid.

LC/MS  $m/z$  206.2 (MH+),  $R_t$  1.88 minutes.

**Ethyl 2-{5-[1-(1,2,4-triazolyl)]benzimidazol-2-yl}acetate**

- The title compound was synthesized as described in Example 7 using
- 20 2-nitro-5-[1-(1,2,4-triazolyl)]phenylamine. LC/MS  $m/z$  272.1 (MH+),  $R_t$  1.19 minutes.

**4-Amino-3-{5-[1-(1,2,4-triazolyl)]benzimidazol-2-yl}hydroquinolin-2-one**

- The title compound was synthesized as described in Example 1, Method A using ethyl 2-{5-[1-(1,2,4-triazolyl)]benzimidazol-2-yl}acetate and
- 25 anthranilonitrile. The crude solid was collected and purified by silica gel chromatography (92:7:1 CH<sub>2</sub>Cl<sub>2</sub>:MeOH:Et<sub>3</sub>N). LC/MS  $m/z$  344.3 (MH+),  $R_t$  2.01 minutes.



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Example 9**Method B**

**N-(4-Chloro-2-cyanophenyl)-2-(5-morpholin-4-ylbenzimidazol-2-yl)acetamide** LiHMDS (2.5 eq) was added to ethyl 2-[5-(2-morpholin-4-yl)benzimidazol-2-yl]acetate (1.0 eq) in THF at -78°C. After 1 hour, 2-amino-5-chlorobenzenecarbonitrile (0.82 eq) in THF was added. The reaction was allowed to warm to 23°C and stirred overnight. The resulting mixture was quenched with NH<sub>4</sub>Cl (aqueous saturated solution) and extracted with EtOAc. The combined organic layers were washed with H<sub>2</sub>O and brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo* to yield a brown solid. The crude material was purified by silica gel chromatography (5:1 EtOAc:hexane) to give the desired product. LC/MS *m/z* 396.1 (MH<sup>+</sup>), R<sub>t</sub> 1.79 minutes.

**4-Amino-6-chloro-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one**  
N-(4-chloro-2-cyanophenyl)-2-(5-morpholin-4-ylbenzimidazol-2-yl)acetamide (1.0 eq) was heated in NaOMe (0.5 M in MeOH, 18 eq) at 70°C for 2 hours. The resulting mixture was cooled, and the resulting solid was filtered and washed with water to give the desired product. LC/MS *m/z* 396.4 (MH<sup>+</sup>), R<sub>t</sub> 2.13 minutes.

Example 10**2-Nitro-5-piperidylphenylamine**

The title compound was synthesized as described in Example 8 using piperidine (3.0 eq, excess acts as base in place of NaH). The desired product was obtained as a yellow, crystalline solid. LC/MS *m/z* 222.2 (MH<sup>+</sup>), R<sub>t</sub> 2.53 minutes.

**Ethyl 2-(5-piperidylbenzimidazol-2-yl)acetate**

The title compound was synthesized as described in Example 7 using 2-nitro-5-piperidylphenylamine. The desired product was obtained as a yellow oil. LC/MS *m/z* 288.3 (MH<sup>+</sup>), R<sub>t</sub> 1.31 minutes.

**4-amino-3-(5-piperidylbenzimidazol-2-yl)hydroquinolin-2-one**

The title compound was synthesized as described in Example 9, Method B using ethyl 2-(5-piperidylbenzimidazol-2-yl)acetate and anthranilonitrile. The acyclic amide was used crude in the NaOMe cyclization step. The desired product was obtained following purification by silica gel chromatography (96.5:3.0:0.5 CH<sub>2</sub>Cl<sub>2</sub>:MeOH:Et<sub>3</sub>N, R<sub>f</sub> 0.2). LC/MS *m/z* 360.4 (MH<sup>+</sup>), R<sub>t</sub> 1.83 minutes.

**Example 11****[1-(3-Amino-4-nitrophenyl)pyrrolidin-3-yl]dimethylamine**

The title compound was synthesized as described in Example 8 using 3-(dimethylamino)pyrrolidine (3.0 eq, excess amine was used as the base in place of NaH). LC/MS *m/z* 251.3 (MH<sup>+</sup>), R<sub>t</sub> 1.25 minutes.

**Ethyl 2-{5-[3-(dimethylamino)pyrrolidinyl]benzimidazol-2-yl}acetate**

The title compound was synthesized as described in Example 7 using [1-(3-amino-4-nitrophenyl)pyrrolidin-3-yl]dimethylamine. The desired product was obtained as a yellow oil. LC/MS *m/z* 317.4 (MH<sup>+</sup>), R<sub>t</sub> 1.36 minutes.

**2-{5-[3-(Dimethylamino)pyrrolidinyl]benzimidazol-2-yl}-N-(4-chloro-2-cyanophenyl)acetamide**

The title compound was synthesized as described in Example 9, Method B using ethyl 2-{5-[3-(dimethylamino)pyrrolidinyl]benzimidazol-2-yl}acetate. LC/MS *m/z* 423.4 (MH<sup>+</sup>), R<sub>t</sub> 1.67 minutes.

**4-Amino-3-{5-[3-(dimethylamino)pyrrolidinyl]benzimidazol-2-yl}-6-chlorohydroquinolin-2-one**

The title compound was synthesized as described in Example 9, Method B using 2-{5-[3-(dimethylamino)pyrrolidinyl]benzimidazol-2-yl}-N-(4-chloro-2-cyanophenyl)acetamide. LC/MS *m/z* 423.4 (MH<sup>+</sup>), R<sub>t</sub> 1.71 minutes.

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**Example 12****Ethyl 2-[5-(dimethylamino)benzimidazol-2-yl]acetate**

The title compound was synthesized as described in Example 7 using (3-amino-4-nitrophenyl)dimethylamine. The resulting tan film was purified by silica gel chromatography (5:1:94 MeOH:Et<sub>3</sub>N:CH<sub>2</sub>Cl<sub>2</sub>) to give the desired product.  
5 LC/MS 248.3 *m/z* (MH<sup>+</sup>), R<sub>t</sub> 1.24 minutes.

**2-[5-(Dimethylamino)benzimidazol-2-yl]-N-(2-cyanophenyl)acetamide**

The title compound was synthesized as described in Example 9, Method B using ethyl 2-[5-(dimethylamino)benzimidazol-2-yl]acetate and  
10 anthranilonitrile. LC/MS *m/z* 320.2 (MH<sup>+</sup>), R<sub>t</sub> 1.68 minutes.

**4-Amino-3-[5-(dimethylamino)benzimidazol-2-yl]hydroquinolin-2-one**

The title compound was synthesized as described in Example 9, Method B using 2-[5-(dimethylamino)benzimidazol-2-yl]-N-(2-cyanophenyl)acetamide. LC/MS *m/z* 320.2 (MH<sup>+</sup>), R<sub>t</sub> 1.72 minutes.

15

**Example 13****Ethyl 2-(5-cyanobenzimidazol-2-yl)acetate**

The title compound was synthesized as described in Example 7 using 4-amino-3-nitro-benzonitrile. LC/MS *m/z* 230.2 (MH<sup>+</sup>), R<sub>t</sub> 1.29 minutes.

**2-(4-Amino-2-oxo-3-hydroquinolyl)benzimidazole-5-carbonitrile**

20

The title compound was synthesized as described in Example 9, Method B using ethyl 2-(5-cyanobenzimidazol-2-yl)acetate and anthranilonitrile (no acyclic amide observed so the NaOMe step was not needed). LC/MS *m/z* 302.3 (MH<sup>+</sup>), R<sub>t</sub> 2.62 minutes.

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Example 14**2-(4-Amino-2-oxo-3-hydroquinolyl)benzimidazole-5-carboxamidine**

2-(4-Amino-2-oxo-3-hydroquinolyl)benzimidazole-5-carbonitrile (1.0 eq) in EtOH was placed into a glass bomb, cooled to 0°C and HCl (g) was bubbled through for 15 minutes. The bomb was then sealed, brought to room temperature and stirred overnight. The solvent was removed *in vacuo*. The residue was dissolved in EtOH in a glass bomb and cooled to 0°C. NH<sub>3</sub> (g) was bubbled through for 15 minutes and the bomb was sealed and heated to 80°C for 5 hours. The solvent was removed *in vacuo* and the crude product was purified by reversed-phase HPLC. LC/MS *m/z* 319.2 (MH<sup>+</sup>), R<sub>t</sub> 1.70 minutes.

Example 15**4-Amino-3-[5-(2-morpholin-4-ylethoxy)-benzimidazol-2-yl]hydroquinolin-2-one**

The title compound was synthesized as described in Example 9, Method B using anthranilonitrile. The crude acyclic amide was used without purification in the NaOMe cyclization step. The crude final product was purified by reversed-phase HPLC (DMSO/5% TFA). LC/MS *m/z* 406.4 (MH<sup>+</sup>), R<sub>t</sub> 1.56 minutes.

Example 16**5-Morpholin-4-yl-2-nitrophenylamine**

The title compound was synthesized as described in Example 8 using morpholine (3.0 eq, excess amine was used as the base in place of NaH). LC/MS *m/z* 224.1 (MH<sup>+</sup>), R<sub>t</sub> 1.89 minutes.

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**Ethyl 2-(5-morpholin-4-ylbenzimidazol-2-yl)acetate**

The title compound was synthesized as described in Example 7 using 5-morpholin-4-yl-2-nitrophenylamine. The crude yellow oil was purified by silica gel chromatography (89.5:10:0.5 CH<sub>2</sub>Cl<sub>2</sub>:MeOH:Et<sub>3</sub>N) to yield the desired product  
5 as a yellow solid. LC/MS *m/z* 290.3 (MH<sup>+</sup>), R<sub>t</sub> 1.31 minutes.

**Method C****4-Hydroxy-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one**

To a solution of ethyl 2-(5-morpholin-4-ylbenzimidazol-2-yl)acetate (1.0 eq) in anhydrous THF at -78°C under an atmosphere of nitrogen was added  
10 LiHMDS (1 M in THF, 3.1 eq) and the solution was stirred for 1 hour. A solution of 1-benzylbenzo[d]1,3-oxazaperhydroine-2,4-dione (1.05 eq) in anhydrous THF was then added dropwise and the resulting solution was allowed to warm to 0°C over 1 hour. The resulting mixture was quenched with a saturated aqueous solution of ammonium chloride and the organic layer was separated. The aqueous layer was  
15 extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 times). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, concentrated *in vacuo*, and the crude material was dissolved in toluene and heated at reflux for 16 hours. The toluene was removed *in vacuo* and the crude material was used without further purification. The product was obtained as a white solid. LC/MS *m/z* 453.1 (MH<sup>+</sup>), R<sub>t</sub> 2.91 minutes.

**20 4-Hydroxy-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one**

Crude 4-hydroxy-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one (1.0 eq) was dissolved in trifluoromethanesulfonic acid and heated at 40°C for 16 hours. The resulting solution was diluted with water and neutralized with 6 N NaOH (aq), whereupon a yellow precipitate formed. The  
25 crude solid was isolated by centrifugation and purified by reversed-phase HPLC to produce the desired product as a bright yellow solid. LC/MS *m/z* 363.3 (MH<sup>+</sup>), R<sub>t</sub> 1.77 minutes.

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**Example 17*****N*-[1-(3-Amino-4-nitrophenyl)pyrrolidin-3-yl](*tert*-butoxy)carboxamide**

The title compound was synthesized as described in Example 8 using 3-(*tert*-butoxycarbonylamino)pyrrolidine (1.01 eq) with diisopropylethylamine (2.0 eq) as the base (in place of NaH). The product was obtained as an orange, crystalline solid. LC/MS *m/z* 323.3 (MH<sup>+</sup>), R<sub>t</sub> 2.53 minutes.

**Ethyl 2-(5-{3-[(*tert*-butoxy)carbonylamino]pyrrolidinyl}benzimidazol-2-yl)acetate**

The title compound was synthesized as described in Example 7 using *N*-[1-(3-amino-4-nitrophenyl)pyrrolidin-3-yl](*tert*-butoxy)carboxamide. The product was obtained as a yellow oil. LC/MS *m/z* 323.3 (MH<sup>+</sup>), R<sub>t</sub> 2.53 minutes.

**3-[5-(3-aminopyrrolidinyl)benzimidazol-2-yl]-4-hydroxyhydroquinolin-2-one**

The title compound was synthesized following the procedure described in Example 16, Method C using ethyl 2-(5-{3-[(*tert*-butoxy)carbonylamino]pyrrolidinyl}benzimidazol-2-yl)acetate. The product was obtained as a yellow solid following cleavage of the benzyl group (see procedure in Example 15). LC/MS *m/e* 362.3 (MH<sup>+</sup>), R<sub>t</sub> 1.55 minutes.

**Example 18****(3-Amino-4-nitrophenyl)[2-(dimethylamino)ethyl]methylamine**

The title compound was synthesized as described in Example 8 using 1,1,4-trimethylethylenediamine (1.01 eq) with diisopropylethylamine (2.0 eq) as the base (in place of NaH). The product was obtained as a bright yellow, crystalline solid. LC/MS *m/z* 239.3 (MH<sup>+</sup>), R<sub>t</sub> 1.29 minutes.

**Ethyl 2-(5-{[2-(dimethylamino)ethyl]methylamino}benzimidazol-2-yl)acetate**

The title compound was synthesized as described in Example 7 using (3-amino-4-nitrophenyl)[2-(dimethylamino)ethyl]methylamine. The desired product was obtained as a yellow oil. LC/MS *m/z* 305.2 (MH<sup>+</sup>), R<sub>t</sub> 1.17 minutes.

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**3-(5-{[2-(Dimethylamino)ethyl]methylamino}benzimidazol-2-yl)-4-hydroxy-1-benzylhydroquinolin-2-one**

The title compound was synthesized as described in Example 16, Method C using ethyl 2-(5-{[2-(dimethylamino)ethyl]methylamino}benzimidazol-2-yl)acetate. The product was obtained as a pale yellow solid. LC/MS *m/z* 468.4 (MH<sup>+</sup>), R<sub>t</sub> 2.26 minutes.

**3-(5-{[2-(Dimethylamino)ethyl]methylamino}benzimidazol-2-yl)-4-hydroxyhydroquinolin-2-one**

The title compound was synthesized as described in Example 16, Method C using 3-(5-{[2-(dimethylamino)ethyl]methylamino}benzimidazol-2-yl)-4-hydroxy-1-benzylhydroquinolin-2-one. The crude material was purified by reversed-phase HPLC to yield the product as a yellow solid. LC/MS *m/z* 378.4 (MH<sup>+</sup>), R<sub>t</sub> 1.99 minutes.

**Example 19****15 Method D****4-Chloro-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one**

A solution of 4-hydroxy-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one (1.0 eq) and POCl<sub>3</sub> in a dry, round-bottomed flask was heated at 80°C for 2 hours. The excess POCl<sub>3</sub> was removed *in vacuo* and the crude material was quenched with water. The crude product was collected by filtration and purified by silica gel chromatography (1:9 MeOH:CH<sub>2</sub>Cl<sub>2</sub>). 4-Chloro-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one was isolated as a red solid. LC/MS *m/z* 471.4 (MH<sup>+</sup>), R<sub>t</sub> 2.35 minutes.

**25 4-[(2-Methoxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one**

A solution of 4-chloro-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one (1.0 eq) and EtOH was treated with 2-methoxyethylamine (10 eq) at room temperature. The resulting solution was heated at reflux for 16 hours and then the solvent was removed *in vacuo*. The crude solid was sonicated

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in water, filtered, sonicated in hexanes, and filtered again. The crude product was used without further purification. LC/MS  $m/z$  510.4 (MH<sup>+</sup>), R<sub>t</sub> 2.20 minutes.

**4-[(2-Methoxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one**

5                    4-[(2-methoxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one was debenzylated using the procedure described in Example 16 to produce the title compound. LC/MS  $m/z$  420.2 (MH<sup>+</sup>), R<sub>t</sub> 1.57 minutes. 4-[(2-hydroxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one was produced as a side product (see below).

10    **4-[(2-hydroxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one**

The title compound was obtained as a side-product of the debenzylation of 4-[(2-methoxyethyl)amino]-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16 and was  
15 isolated by reversed-phase HPLC as a yellow solid. LC/MS  $m/z$  406.2 (MH<sup>+</sup>), R<sub>t</sub> 1.39 minutes.

#### Example 20

**4-(Methoxyamino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one**

20                    The title compound was synthesized as described in Example 19, Method D using *O*-methylhydroxylamine. The product was used without purification.

**4-(Methoxyamino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one**

The title compound was obtained as a yellow solid after debenzylation  
25 of 4-(methoxyamino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16. LC/MS  $m/z$  392.2 (MH<sup>+</sup>), R<sub>t</sub> 1.82 minutes.



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**Example 21**

***tert*-Butyl-3-{[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}piperidinecarboxylate**

- The title compound was synthesized as described in Example 19,  
5 Method D using 1-*tert*-butoxycarbonyl-3-aminopiperidine. The product was used without purification.

**3-(5-Morpholin-4-ylbenzimidazol-2-yl)-4-(3-piperidylamino)hydroquinolin-2-one**

- The product was obtained as a yellow solid after debenzylation of  
*tert*-butyl-3-{[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-  
10 hydroquinolyl]amino}piperidinecarboxylate using the procedure described in Example 16. The *t*-butoxycarbonyl group is removed under the reaction conditions. LC/MS *m/z* 445.4 (MH<sup>+</sup>), R<sub>t</sub> 1.73 minutes.

**Example 22**

- tert*-Butyl-3-({[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-  
15 hydroquinolyl]amino}methyl)piperidinecarboxylate**

The title compound was synthesized as described in Example 19,  
Method D using 1-*tert*-butoxycarbonyl-3-aminomethylpiperidine. The product was used without purification.

- 3-(5-Morpholin-4-ylbenzimidazol-2-yl)-4-[(3-piperidylmethyl)amino]-  
20 hydroquinolin-2-one**

The title compound was obtained as a yellow solid after debenzylation of *tert*-butyl-3-({[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}methyl)piperidinecarboxylate using the procedure described in Example 16. LC/MS *m/z* 459.6 (MH<sup>+</sup>), R<sub>t</sub> 1.71 minutes.

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**Example 23**

**4-{[2-(Dimethylamino)ethyl]amino}-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one**

- The title compound was synthesized as described in Example 19,  
5 Method D using 1,1-dimethylethylenediamine. The product was used without purification.

**4-{[2-(Dimethylamino)ethyl]amino}-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one**

- The title compound was obtained as a yellow solid after debenzylation  
10 of 4-{[2-(dimethylamino)ethyl]amino}-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16. LC/MS *m/z* 433.4 (MH<sup>+</sup>), R<sub>t</sub> 1.55 minutes.

**Example 24**

- 3-(5-Morpholin-4-ylbenzimidazol-2-yl)-4-[(oxolan-2-ylmethyl)amino]-1-benzylhydroquinolin-2-one**  
15

The title compound was synthesized as described in Example 19,  
Method D using 2-aminomethyltetrahydrofuran. The product was used without purification.

- 3-(5-Morpholin-4-ylbenzimidazol-2-yl)-4-[(oxolan-2-ylmethyl)amino]-hydroquinolin-2-one**  
20

The title compound was obtained as a yellow solid after debenzylation  
of 3-(5-morpholin-4-ylbenzimidazol-2-yl)-4-[(oxolan-2-ylmethyl)amino]-1-benzylhydroquinolin-2-one using the procedure described in Example 16. LC/MS *m/z* 446.5 (MH<sup>+</sup>), R<sub>t</sub> 2.19 minutes.

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Example 25

4-{[2-(Methylamino)ethyl]amino}-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one

- The title compound was synthesized as described in Example 19,  
5 Method D using 1-*tert*-butoxycarbonyl-1-methylethylenediamine. The product was used without purification.

4-{[2-(Methylamino)ethyl]amino}-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one

- The title compound was obtained as a yellow solid after debenzylation  
10 of 4-{[2-(methylamino)ethyl]amino}-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16. The *t*-butoxycarbonyl group is removed under the reaction conditions. LC/MS *m/z* 419.4 (MH<sup>+</sup>), R<sub>t</sub> 1.50 minutes.

Example 26

- 15 *tert*-Butyl-3-{[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}pyrrolidinecarboxylate

The title compound was synthesized as described in Example 19,  
Method D using 1-*tert*-butoxycarbonyl-3-aminopyrrolidine. The product was used without purification.

- 20 3-(5-Morpholin-4-ylbenzimidazol-2-yl)-4-(pyrrolidin-3-ylamino)hydroquinolin-2-one

- The title compound was obtained as a yellow solid after debenzylation  
of *tert*-butyl-3-{[3-(5-morpholin-4-ylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}pyrrolidinecarboxylate using the procedure described in  
25 Example 16. LC/MS *m/z* 431.4 (MH<sup>+</sup>), R<sub>t</sub> 1.50 minutes.

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Example 27

4-(((2*S*)-2-Amino-4-methylpentyl)amino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one

The title compound was synthesized as described in Example 19,

- 5 Method D using (2*S*)-2-*tert*-butoxycarbonylamino-4-methylpentylamine. The product was used without purification.

4-(((2*S*)-2-Amino-4-methylpentyl)amino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one

- 10 The title compound was obtained as a yellow solid after debenzylation of 4-(((2*S*)-2-amino-4-methylpentyl)amino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16. LC/MS *m/z* 461.4 (MH<sup>+</sup>), R<sub>t</sub> 1.78 minutes.

Example 28

- 15 *t*-Butoxycarbonyl protected 4-(((2*S*)-2-amino-3-methylbutyl)amino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one

The title compound was synthesized as described in Example 19, Method D using (2*S*)-2-*tert*-butoxycarbonylamino-3-methylbutylamine. The product was used without purification.

- 20 4-(((2*S*)-2-Amino-3-methylbutyl)amino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one

- The title compound was obtained as a yellow solid after debenzylation of 4-(((2*S*)-2-amino-3-methylbutyl)amino)-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16. The *t*-butoxycarbonyl group is removed under the reaction conditions. LC/MS *m/z* 447.5  
25 (MH<sup>+</sup>), R<sub>t</sub> 2.96 minutes.

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**Example 29****4-Amino-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one**

The title compound was synthesized as described in Example 19, Method D using ammonia in a sealed glass tube. The product was used without  
5 purification.

**4-Amino-3-(5-morpholin-4-ylbenzimidazol-2-yl)hydroquinolin-2-one**

The title compound was obtained as a bright yellow solid after debenzilation of 4-amino-3-(5-morpholin-4-ylbenzimidazol-2-yl)-1-benzylhydroquinolin-2-one using the procedure described in Example 16 and  
10 purification by reversed-phase HPLC. LC/MS *m/z* 362.3 (MH<sup>+</sup>), R<sub>t</sub> 1.61 minutes.

**Example 30****3-Benzimidazol-2-yl-4-hydroxy-1-benzylhydroquinolin-2-one**

The title compound was synthesized as described in Example 16, Method C using ethyl 2-benzimidazol-2-ylacetate. The product was obtained as a  
15 white solid and used without further purification. LC/MS *m/z* 368.4 (MH<sup>+</sup>), R<sub>t</sub> 2.99 minutes.

**3-(Benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one**

The title compound was synthesized as described in Example 19, Method D using 3-benzimidazol-2-yl-4-hydroxy-1-benzylhydroquinolin-2-one. The  
20 crude product was used without purification.

**Example 31****3-Benzimidazol-2-yl-4-(methyldamino)hydroquinolin-2-one**

The benzylated title compound was synthesized as described in Example 19, Method D using methylamine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The product was obtained after debenzilation as a  
25 yellow solid using the procedure described in Example 16. LC/MS *m/z* 291.3 (MH<sup>+</sup>), R<sub>t</sub> 1.64 minutes.

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Example 32**3-Benzimidazol-2-yl-4-(ethylamino)hydroquinolin-2-one**

The benzylated title compound was synthesized as described in Example 19, Method D using ethylamine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS *m/z* 305.3 (MH<sup>+</sup>), R<sub>t</sub> 2.01 minutes.

Example 33**3-Benzimidazol-2-yl-4-[(oxolan-2-ylmethyl)amino]hydroquinolin-2-one**

The benzylated title compound was synthesized as described in Example 19, Method D using 2-aminomethyltetrahydrofuran and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS *m/z* 361.2 (MH<sup>+</sup>), R<sub>t</sub> 1.74 minutes.

Example 34**3-Benzimidazol-2-yl-4-[(4-piperidylmethyl)amino]hydroquinolin-2-one**

The protected title compound was synthesized as described in Example 19, Method D using 1-*tert*-butoxycarbonyl-4-aminomethylpiperidine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after deprotection and debenzylation as a yellow solid using the procedure described in Example 16. LC/MS *m/z* 374.3 (MH<sup>+</sup>), R<sub>t</sub> 1.29 minutes.

Example 35**3-Benzimidazol-2-yl-4-[(4-fluorophenyl)amino]hydroquinolin-2-one**

The benzylated title compound was synthesized as described in Example 19, Method D using 4-fluoroaniline and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as

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a yellow solid using the procedure described in Example 16. LC/MS  $m/z$  371.2 (MH<sup>+</sup>), R<sub>t</sub> 1.92 minutes.

#### Example 36

##### **3-Benzimidazol-2-yl-4-(methoxyamino)hydroquinolin-2-one**

5                   The benzylated title compound was synthesized as described in Example 19, Method D using *O*-methylhydroxylamine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS  $m/z$  307.3 (MH<sup>+</sup>), R<sub>t</sub> 1.77 minutes.

#### Example 37

##### **3-Benzimidazol-2-yl-4-(benzimidazol-6-ylamino)hydroquinolin-2-one**

10                   The benzylated title compound was synthesized as described in Example 19, Method D using 5-aminobenzimidazole and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after  
15 debenzylation as a yellow solid using the procedure described in Example 16. LC/MS  $m/z$  393.4 (MH<sup>+</sup>), R<sub>t</sub> 1.41 minutes.

#### Example 38

##### **3-Benzimidazol-2-yl-4-(phenylamino)hydroquinolin-2-one**

20                   The benzylated title compound was synthesized as described in Example 19, Method D using aniline and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS  $m/z$  353.4 (MH<sup>+</sup>), R<sub>t</sub> 2.38 minutes.

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**Example 39****3-Benzimidazol-2-yl-4-(quinuclidin-3-ylamino)hydroquinolin-2-one**

The benzylated title compound was synthesized as described in Example 19, Method D using 3-aminoquinuclidine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS  $m/z$  386.4 (MH<sup>+</sup>), R<sub>t</sub> 1.82 minutes.

**Example 40****3-Benzimidazol-2-yl-4-[(imidazol-5-ylmethyl)amino]hydroquinolin-2-one**

The benzylated title compound was synthesized as described in Example 19, Method D using 4-aminomethyl-1H-imidazole and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS  $m/z$  357.4 (MH<sup>+</sup>), R<sub>t</sub> 1.34 minutes.

**Example 41****3-Benzimidazol-2-yl-4-(morpholin-4-ylamino)hydroquinolin-2-one**

The benzylated title compound was synthesized as described in Example 19, Method D using 4-aminomorpholine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained after debenzylation as a yellow solid using the procedure described in Example 16. LC/MS  $m/z$  362.4 (MH<sup>+</sup>), R<sub>t</sub> 1.42 minutes.

**Example 42****3-Benzimidazol-2-yl-4-hydrazinohydroquinolin-2-one**

The benzylated title compound was synthesized as described in Example 19, Method D using hydrazine and 3-(benzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one. The title compound was obtained as a yellow solid after



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debenzylation using the procedure described in Example 16. LC/MS  $m/z$  292.3 (MH<sup>+</sup>), R<sub>t</sub> 1.19 minutes.

#### Example 43

##### **3-Benzimidazol-2-yl-2-oxohydroquinoline-4-carbonitrile**

5                    3-Benzimidazol-2-yl-4-chloro-1-benzylhydroquinolin-2-one (1 eq) was dissolved in DMA, and CuCN (10 eq) was added in one portion. The reaction mixture was stirred at 90°C overnight. The resulting mixture was allowed to cool to room temperature, water was added, and the orange precipitate was removed by filtration. The solid was treated with a solution of hydrated FeCl<sub>3</sub> at 70°C for 1  
10 hour. The suspension was centrifuged and the solution removed. The remaining solid was washed with 6N HCl (2 times), sat. Na<sub>2</sub>CO<sub>3</sub> (2 times), water (2 times) and lyophilized. The resulting powder was dissolved in 1 mL of triflic acid and heated at 60°C overnight. The resulting mixture was cooled to 0°C and water was slowly added. Saturated LiOH was added dropwise to the suspension to a pH of 8, then the  
15 solid was filtered and washed with water (3 times). Purification by reversed-phase HPLC afforded the desired product. LC/MS  $m/z$  287.1 (MH<sup>+</sup>), R<sub>t</sub> 1.89 minutes.

#### Example 44

##### **Ethyl 2-(5,6-dimethylbenzimidazol-2-yl)acetate**

The title compound was synthesized as described in Example 1 using  
20 4,5-dimethylbenzene-1,2-diamine. The crude yellow oil was purified first by silica gel chromatography (96.5:3.0:0.5, CH<sub>2</sub>Cl<sub>2</sub>:MeOH:Et<sub>3</sub>N), and then by recrystallization from toluene to yield the title compound as a pale, yellow solid. LC/MS  $m/z$  233.1 (MH<sup>+</sup>), R<sub>t</sub> 1.73 minutes.

##### **3-(5,6-Dimethylbenzimidazol-2-yl)-4-hydroxy-1-benzylhydroquinolin-2-one**

25                    The title compound was synthesized as described in Example 16, Method C using ethyl 2-(5,6-dimethylbenzimidazol-2-yl)acetate. The crude material was purified by silica gel chromatography (98.5:1.5, CH<sub>2</sub>Cl<sub>2</sub>:MeOH) to yield the title compound as a yellow solid. LC/MS  $m/z$  396.2 (MH<sup>+</sup>), R<sub>t</sub> 3.60 minutes.

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**3-(5,6-Dimethylbenzimidazol-2-yl)-4-chloro-1-benzylhydroquinolin-2-one**

The title compound was synthesized as described in Example 19, Method D using 3-(5,6-dimethylbenzimidazol-2-yl)-4-hydroxy-1-benzylhydroquinolin-2-one. The title compound was obtained as an orange-yellow solid. LC/MS  $m/z$  414.2 (MH<sup>+</sup>), R<sub>t</sub> 2.47 minutes.

***tert*-Butyl 3-{[3-(5,6-dimethylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}piperidinecarboxylate**

The title compound was synthesized as described in Example 19, Method D using 1-*tert*-butoxycarbonyl-3-aminopiperidine. The crude material was purified by silica gel chromatography (99:1 CH<sub>2</sub>Cl<sub>2</sub>:MeOH) to yield the title compound as a yellow solid. LC/MS  $m/z$  578.5 (MH<sup>+</sup>), R<sub>t</sub> 3.05 minutes.

**3-(5,6-Dimethylbenzimidazol-2-yl)-4-(3-piperidylamino)hydroquinolin-2-one**

*tert*-Butyl 3-{[3-(5,6-dimethylbenzimidazol-2-yl)-2-oxo-1-benzyl-4-hydroquinolyl]amino}piperidine-carboxylate was debenzylated as described in Example 16. The crude material was purified by reversed-phase HPLC to yield the title compound as a light yellow solid. LC/MS  $m/z$  388.4 (MH<sup>+</sup>), R<sub>t</sub> 1.61 minutes.

**Example 45****3*H*-Imidazo[4,5-*b*]pyridin-2-ylacetonitrile**

Ethyl cyanoacetate (1.5 eq) and 2,3-diaminopyridine (1 eq) were heated at 185°C for 30 minutes. The reaction mixture was cooled to room temperature and the black solid was triturated with ether. The desired product was thus obtained as a dark brown powder. LC/MS  $m/z$  159.1 (MH<sup>+</sup>), R<sub>t</sub> 0.44 minutes.

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**Ethyl 3*H*-imidazo[4,5-*b*]pyridin-2-ylacetate**

3*H*-Imidazo[4,5-*b*]pyridin-2-ylacetonitrile was suspended in EtOH, and gaseous HCl was bubbled through for 3 hours. The suspension initially seemed to dissolve, but a precipitate started forming almost immediately. The reaction  
5 mixture was cooled to 0°C and a cold saturated NaHCO<sub>3</sub> solution was carefully added. Solid NaHCO<sub>3</sub> was also added to bring the pH to a value of 7.6. The aqueous phase was then extracted with EtOAc, and the organic extracts were dried (Na<sub>2</sub>SO<sub>4</sub>). After evaporation of the solvent under reduced pressure, the residue was purified by chromatography on silicagel (10% MeOH in CH<sub>2</sub>Cl<sub>2</sub> with 1% Et<sub>3</sub>N)  
10 providing the desired product as a light brown solid. LC/MS *m/z* 206.1 (MH<sup>+</sup>), R<sub>t</sub> 0.97 minutes.

**4-Amino-3-(3*H*-imidazo[4,5-*b*]pyridin-2-yl)quinolin-2(1*H*)-one**

LiHMDS (3.0 eq) was added to ethyl 3*H*-imidazo[4,5-*b*]pyridin-2-ylacetate (1.0 eq) in THF at -78°C. After 20 minutes, a solution of 2-  
15 aminobenzenecarbonitrile (1.1 eq) in THF was added. The resulting mixture was allowed to warm to room temperature, stirred for 3 hours, and then refluxed overnight. The mixture was cooled to 0°C and quenched with an aqueous saturated NH<sub>4</sub>Cl solution. A precipitate formed, was filtered off, and was washed repeatedly with ether to yield the desired compound as a light brown solid. LC/MS *m/z* 278.2  
20 (MH<sup>+</sup>), R<sub>t</sub> 1.82 minutes.

**Example 46****6-Morpholin-4-yl-3-nitropyridin-2-amine**

Morpholine (4 eq) was added to a suspension of 6-chloro-3-nitropyridin-2-amine (1 eq) in CH<sub>3</sub>CN, and the reaction mixture was stirred at  
25 70°C for 5 hours. The solvent was evaporated under reduced pressure, and the residue was triturated with ether to afford the desired compound as a bright yellow powder. LC/MS *m/z* 225.0 (MH<sup>+</sup>), R<sub>t</sub> 1.79 minutes.

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**Ethyl (5-morpholin-4-yl-3H-imidazo[4,5-b]pyridin-2-yl)acetate**

To a solution 6-chloro-3-nitropyridin-2-amine (1.0 eq) in EtOH was added Pd/C (0.1 eq). The reaction vessel was repeatedly purged with hydrogen and then stirred under a hydrogen atmosphere (1 atm) for 18 hours. Ethyl 3-ethoxy-3-  
5 iminopropanoate hydrochloride (2.0 eq) was added in one portion, and the reaction mixture was refluxed overnight. The reaction mixture was cooled to room temperature, filtered through a celite plug, and the plug was washed with EtOH. After evaporation of the solvent under reduced pressure, the residue was purified by silica gel chromatography (5% MeOH in CH<sub>2</sub>Cl<sub>2</sub> with 1% Et<sub>3</sub>N) providing the  
10 desired product as a brown solid. LC/MS *m/z* 291.3 (MH<sup>+</sup>), R<sub>t</sub> 1.71 minutes.

**4-Amino-3-(5-morpholin-4-yl-3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one**

The title compound was synthesized as described in Example 45, Method E using ethyl 2-(5-morpholin-4-ylimidazolo[5,4-b]pyridin-2-yl)acetate and 2-aminobenzenecarbonitrile, with a modified workup procedure.. After quenching  
15 with a saturated aqueous ammonium chloride solution, the two phases were separated and the aqueous phase extracted with EtOAc. Upon standing, a solid formed and precipitated out of the organic extracts. The precipitate, a dark brown solid, was filtered off and dried. Purification by reverse phase chromatography afforded the desired product as a reddish solid. LC/MS *m/z* 363.2 (MH<sup>+</sup>), R<sub>t</sub> 2.20  
20 minutes.

**Example 47****4-Amino-5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one**

LiHMDS (3.0 eq) was added to ethyl 3H-imidazo[4,5-b]pyridin-2-ylacetate (1.0 eq) in THF at -78°C. After 20 minutes, a solution of 2-amino-6-  
25 [(2R,6S)-2,6-dimethylmorpholin-4-yl]benzonitrile (1.1 eq) in THF was added. The resulting mixture was allowed to warm to room temperature, stirred for 2 hours and then heated to 60°C overnight. The mixture was cooled to 0°C and quenched with an aqueous saturated NH<sub>4</sub>Cl solution. The aqueous phase was extracted with

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CH<sub>2</sub>Cl<sub>2</sub> (5 times) and the organic extracts were collected, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. The crude product was purified by HPLC. LC/MS *m/z* 391.2 (MH<sup>+</sup>), R<sub>t</sub> 2.35 minutes.

#### Example 48

5 **Ethyl {5-[3-(dimethylamino)pyrrolidin-1-yl]-3*H*-imidazo[4,5-*b*]pyridin-2-yl}acetate**

6-chloro-3-nitro-2-aminopyridine (1.0 eq) and 3-(dimethylamino)pyrrolidine (1.1 eq) were dissolved in CH<sub>3</sub>CN and diisopropylethylamine (2.0 eq) was added. The reaction mixture was heated at 70°C overnight. The solution was cooled to room temperature, and the solvent was evaporated. The residue was triturated with ether and water and dried under vacuum (LC/MS *m/z* 252.2 (MH<sup>+</sup>), R<sub>t</sub> 1.09 minutes). The isolated product (1.0 eq) and 10% Pd/C (0.1 eq) were suspended in anhydrous EtOH at room temperature. The reaction flask was evacuated and subsequently filled with H<sub>2</sub>.  
15 The resulting mixture was allowed to stir under a hydrogen atmosphere overnight. Ethyl 3-ethoxy-3-iminopropanoate hydrochloride (2.0 eq) was then added and the resulting mixture was heated at reflux overnight. The solution was then filtered through Celite and evaporated under reduced pressure. The residue was suspended in CH<sub>2</sub>Cl<sub>2</sub> and concentrated NH<sub>4</sub>OH was added until a pH of 11 was achieved. The  
20 NH<sub>4</sub>Cl thus formed was filtered off. The two phases were separated, and the organic phase was dried (Na<sub>2</sub>SO<sub>4</sub>). Evaporation of the solvent and trituration of the residue with ether gave a light green powder. LC/MS *m/z* 318.1 (MH<sup>+</sup>), R<sub>t</sub> 1.11 minutes.

25 **4-Amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-3*H*-imidazo[4,5-*b*]pyridin-2-yl}quinolin-2(1*H*)-one**

LiHMDS (3.5 eq) was added to ethyl {5-[3-(dimethylamino)pyrrolidin-1-yl]-3*H*-imidazo[4,5-*b*]pyridin-2-yl}acetate (1.0 eq) in THF at -40 °C. After 10 minutes, a solution of 2-aminobenzonitrile (1.1

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eq) in THF was added. The resulting mixture was allowed to warm to room temperature, stirred for 1 h and then heated to 60 °C overnight. The mixture was cooled to room temperature and quenched with NH<sub>4</sub>Cl (aq, saturated). The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 times). The product crashes out of the organic solution during the extractions. Evaporation of the solvent under reduced pressure afforded a brown solid that was triturated repeatedly with MeOH and acetone to obtain a yellow greenish powder. LC/MS *m/z* 390.2 (MH<sup>+</sup>), R<sub>t</sub> 1.48 minutes.

#### Example 49

##### 2-(4-Ethylpiperazinyl)-6-nitrobenzenecarbonitrile

10                    2,6-Dinitrobenzenecarbonitrile (1.0 eq) and ethylpiperazine (3.6 eq) were dissolved in DMF. The resulting solution heated at 90 °C for 2 hours. The solution was cooled to room temperature and poured into H<sub>2</sub>O. A precipitate formed which was filtered to yield the desired product as a brown solid. LC/MS *m/z* 260.1 (MH<sup>+</sup>), R<sub>t</sub> 1.69 minutes.

##### 15    6-Amino-2-(4-ethylpiperazinyl)benzenecarbonitrile

                    2-(4-Ethylpiperazinyl)-6-nitrobenzenecarbonitrile (1.0 eq) was dissolved in EtOH and EtOAc. The flask was purged with N<sub>2</sub>, and 10% Pd/C (0.1 eq) was added. The flask was evacuated and purged with H<sub>2</sub> three times. The resulting mixture was stirred overnight at room temperature. The mixture was  
20 filtered through Celite, and the filter pad was washed with EtOAc. The solvent was removed *in vacuo* to provide the desired product as a yellow solid. LC/MS *m/z* 231.2 (MH<sup>+</sup>), R<sub>t</sub> 1.42 minutes.

##### 4-Amino-3-(1H-benzimidazol-2-yl)-5-(4-ethylpiperazin-1-yl)quinolin-2(1H)-one

*t*-BuLi (3.1 eq) was added to ethyl 2-benzimidazol-2-ylacetate (1.0  
25 eq) and 6-amino-2-(4-ethylpiperazinyl)benzenecarbonitrile (1.0 eq) in THF at 0 °C. The reaction was stirred overnight. The resulting mixture was quenched with NH<sub>4</sub>Cl (aq, saturated) and extracted with EtOAc. The combined organic layers were washed with H<sub>2</sub>O and brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated *in*

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*vacuo* to yield a brown solid. The crude material was triturated with  $\text{CH}_2\text{Cl}_2$  and MeOH to provide a tan solid. LC/MS  $m/z$  389.1 (MH<sup>+</sup>), R<sub>t</sub> 1.80 minutes.

### Examples 50-154

The 2-aminobenzonitriles or isatoic anhydride starting materials used to synthesize Examples 50-154 are readily recognizable by one skilled in the art. They were either commercially available or synthesized following the examples shown above (e.g. Examples 1, 2, and 49). The anhydride 6-chloro-1-(phenylmethyl)-2H-3,1-benzoxazine-2,4(1H)-dione was synthesized following the general isatoic anhydride synthesis methods described in *J. Med. Chem.* 1981, 24 (6), 735 and *J. Heterocycl. Chem.* 1975, 12(3), 565.

The benzimidazole acetates were formed by reacting aryl diamines with ethyl 3-ethoxy-3-iminopropanoate hydrochloride as shown in Example 1. The requisite diamines used in the syntheses are also readily recognizable by one skilled in the art and may be synthesized following Methods 1-9. The isatoic anhydrides were coupled with the benzimidazole acetates using methods C and D. The 2-aminobenzonitriles were coupled with the benzimidazole acetates using method B, the coupling method of example 49, or the general procedure set forth below.

**Method E**

LiHMDS (3-4 eq) was added to the benzimidazole acetate (1.0 eq) in THF (at a constant temperature ranging from  $-78^{\circ}\text{C}$  to  $0^{\circ}\text{C}$ ). After 20 minutes, a solution of the 2-aminobenzonitrile (1.1 eq) in THF was then added. The resulting mixture was allowed to warm to room temperature, stirred for 1-3 hours and was then heated to approx.  $40^{\circ}\text{C}$  -  $65^{\circ}\text{C}$  (1 hour to 12 hours). The mixture was cooled to  $0^{\circ}\text{C}$  and quenched with  $\text{NH}_4\text{Cl}$  (aq, saturated). The aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  or EtOAc, and the organic extracts were collected, dried ( $\text{Na}_2\text{SO}_4$ ), and filtered. Evaporation of the solvent under reduced pressure and purification of the residue by silica gel chromatography or HPLC provided the 4-amino quinolinone products.

Example	Name	LC/MS m/z (MH+)
50	4-amino-3-{5-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	389.4
51	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-chloroquinolin-2(1H)-one	420
52	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-chloroquinolin-2(1H)-one	420
53	3-(1H-benzimidazol-2-yl)-4-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]quinolin-2(1H)-one	374.2
54	3-(1H-benzimidazol-2-yl)-6-chloro-4-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]quinolin-2(1H)-one	408.1
55	4-amino-3-[5-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1-methylquinolin-2(1H)-one	403.2
56	4-amino-3-(6-piperazin-1-yl)-1H-benzimidazol-2-ylquinolin-2(1H)-one	361.2
57	4-amino-3-[6-(pyridin-4-ylmethyl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	368.2
58	4-amino-3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	389.4



59	4-amino-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	375.2
60	4-amino-3-(6-methyl-5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	376
61	4-amino-3-{5-[(1-methylpiperidin-3-yl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	390.1
62	4-amino-3-{5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one	408.2
63	4-amino-3-{5-[(1-methylpyrrolidin-3-yl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	376.2
64	4-amino-3-[5-(4-methyl-1,4-diazepan-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	389.2
65	4-amino-3-{5-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	389.2
66	4-amino-6-chloro-3-{5-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	423
67	ethyl {4-[2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-6-yl]piperazin-1-yl}acetate	447.2
68	4-amino-3-{6-[methyl(1-methylpiperidin-4-yl)amino]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	403.1
69	3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-aminoquinolin-2(1H)-one	403.3
70	4-amino-3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	443.3
71	2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazole-6-carboxylic acid	321.2
72	4-amino-5-(methyloxy)-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	405.3
73	4-amino-3-{6-[4-(1-methylethyl)piperazin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	403.3
74	{4-[2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-6-yl]piperazin-1-yl}acetic acid	419.2
75	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)quinolin-2(1H)-one	386.1
76	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)quinolin-2(1H)-one	386.1
77	4-amino-3-[5-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	389.1

78	4-amino-3-(5-((2S,5S)-2-[(dimethylamino)methyl]-5-methylmorpholin-4-yl)-1H-benzimidazol-2-yl)quinolin-2(1H)-one	433.3
79	4-amino-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	409.2
80	4-amino-6-chloro-3-[5-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one	423.1
81	4-amino-5,6-dichloro-3-[5-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one	457.2
82	4-amino-5,6-dichloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	443.2
83	4-amino-3-(1H-benzimidazol-2-yl)-6-[(pyridin-2-ylmethyl)oxy]quinolin-2(1H)-one	384.2
84	4-amino-3-(1H-benzimidazol-2-yl)-6-[(2R,6S)-2,6-dimethylmorpholin-4-yl]quinolin-2(1H)-one	390.1
85	4-amino-3-(1H-benzimidazol-2-yl)-6-morpholin-4-ylquinolin-2(1H)-one	362.2
86	4-amino-3-(1H-benzimidazol-2-yl)-5-[(1-methylpiperidin-3-yl)oxy]quinolin-2(1H)-one	390.2
87	4-amino-3-(1H-benzimidazol-2-yl)-5-[(pyridin-2-ylmethyl)oxy]quinolin-2(1H)-one	384.1
88	4-amino-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-5-[(pyridin-4-ylmethyl)oxy]quinolin-2(1H)-one	469.2
89	4-amino-3-(1H-benzimidazol-2-yl)-5-(methyloxy)quinolin-2(1H)-one	307.1
90	4-amino-3-(5-methyl-1H-benzimidazol-2-yl)-5-(methyloxy)quinolin-2(1H)-one	321.1
91	4-amino-3-[5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-1H-benzimidazol-2-yl]-5-(methyloxy)quinolin-2(1H)-one	420.2
92	4-amino-3-(1H-benzimidazol-2-yl)-5-morpholin-4-ylquinolin-2(1H)-one	362.2
93	4-amino-3-(1H-benzimidazol-2-yl)-5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]quinolin-2(1H)-one	390.2
94	4-amino-3-(1H-benzimidazol-2-yl)-5-(4-methylpiperazin-1-yl)quinolin-2(1H)-one	375.1
95	4-amino-5,6-dichloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	430

96	3-{5-[(2-morpholin-4-ylethyl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	391.3
97	4-amino-3-{5-[(3-pyrrolidin-1-ylpropyl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	404
98	4-amino-3-{5-[(3-morpholin-4-ylpropyl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	420.4
99	4-amino-6-fluoro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	380
100	4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}-6-fluoroquinolin-2(1H)-one	407
101	4-amino-3-(1H-benzimidazol-2-yl)-6-fluoroquinolin-2(1H)-one	295
102	4-amino-3-(6-fluoro-5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	380
103	4-amino-3-{5-[(tetrahydrofuran-2-ylmethyl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one	377
104	4-amino-6-fluoro-3-(6-fluoro-5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	398
105	4-amino-3-[6-fluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	393
106	4-amino-3-(5-{[2-(methyloxy)ethyl]oxy}-1H-benzimidazol-2-yl)quinolin-2(1H)-one	351
107	4-amino-3-[4,6-difluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	411
108	4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}-5-fluoroquinolin-2(1H)-one	407.1
109	4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	393.1
110	4-amino-5-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	409.1
111	4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one	407.1
112	4-amino-5-chloro-3-[5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one	423.1
113	4-amino-6-chloro-3-[5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl]quinolin-2(1H)-one	441

114	4-amino-5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one	391.2
115	4-amino-3-(6-thiomorpholin-4-yl)-1H-benzimidazol-2-ylquinolin-2(1H)-one	378.4
116	4-amino-3-[5-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	443.1
117	4-amino-3-[6-[3-(diethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one	417.1
118	4-amino-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	438.3
119	4-amino-3-[5-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one	376.3
120	4-amino-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one	410.2
121	2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N-methyl-N-(1-methylpiperidin-4-yl)-1H-benzimidazole-5-carboxamide	431.3
122	4-amino-3-(5-[[4-(1-methylethyl)piperazin-1-yl]carbonyl]-1H-benzimidazol-2-yl)quinolin-2(1H)-one	431.3
123	4-amino-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6-nitroquinolin-2(1H)-one	420.2
124	4-amino-3-[5-(1,4'-bipiperidin-1'-ylcarbonyl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	471.1
125	4-amino-3-[5-[(4-methylpiperazin-1-yl)carbonyl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one	403.3
126	4-amino-3-[5-(1-oxidothiomorpholin-4-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	394.5
127	3-[5-[(4-acetylpiperazin-1-yl)carbonyl]-1H-benzimidazol-2-yl]-4-aminoquinolin-2(1H)-one	431.3
128	4-amino-3-(5-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl)-1H-benzimidazol-2-ylquinolin-2(1H)-one	417.4

129	4-amino-3-(5-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl)-1H-benzimidazol-2-yl)quinolin-2(1H)-one	417.4
130	4-amino-3-(5-[[4-(dimethylamino)piperidin-1-yl]carbonyl]-1H-benzimidazol-2-yl)quinolin-2(1H)-one	431.4
131	methyl 2-(4-amino-5-fluoro-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazole-6-carboxylate	353.2
132	4-amino-3-[5-(1,3'-bipyrrolidin-1'-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	415.5
133	4-amino-3-[5-(pyridin-3-yloxy)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	370.2
134	4-amino-5,6-bis(methyloxy)-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	435.5
135	2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N-[2-(dimethylamino)ethyl]-N-methyl-1H-benzimidazole-5-carboxamide	405.3
136	2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N-methyl-N-(1-methylpyrrolidin-3-yl)-1H-benzimidazole-5-carboxamide	417.2
137	4-amino-3-[5-[(5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl)carbonyl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one	415.2
138	4-amino-3-[5-[(4-cyclohexylpiperazin-1-yl)carbonyl]-1H-benzimidazol-2-yl]quinolin-2(1H)-one	471.6
139	4-amino-3-[5-[(2-piperidin-1-ylethyl)amino]-1H-benzimidazol-2-yl]quinolin-2(1H)-one	403.2
140	ethyl 4-[[2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-5-yl]amino]piperidine-1-carboxylate	447.3
141	4-amino-3-[5-(((5R)-5-((methyloxy)methyl)pyrrolidin-3-yl)amino)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	405.2
142	4-amino-3-[5-[(pyridin-2-ylmethyl)amino]-1H-benzimidazol-2-yl]quinolin-2(1H)-one	383.3
143	4-amino-3-[5-(piperidin-3-ylamino)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	375.2
144	4-amino-5-fluoro-3-[5-[(pyridin-2-ylmethyl)amino]-1H-benzimidazol-2-yl]quinolin-2(1H)-one	401.3

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145	ethyl 4-[[2-(4-amino-5-fluoro-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-5-yl]amino]piperidine-1-carboxylate	465.5
146	4-amino-5-fluoro-3-[5-(piperidin-3-ylamino)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	393.3
147	4-amino-3-(1H-benzimidazol-2-yl)-6-bromoquinolin-2(1H)-one	357.1
148	4-amino-3-(1H-benzimidazol-2-yl)-7-bromoquinolin-2(1H)-one	357.1
149	4-amino-3-(5-bromo-1H-benzimidazol-2-yl)quinolin-2(1H)-one	357.1
150	N,N-dimethyl-2-(2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazole-5-carboxamide	333.1
151	4-amino-3-(5-thien-2-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	359.2
152	2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N,N-dimethyl-1H-benzimidazole-5-sulfonamide	384.1
153	4-amino-6-iodo-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	501.1
154	4-amino-3-(5-{2-[(dimethylamino)methyl]-morpholin-4-yl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one	419.2

### Examples 155-270

Examples 155 to 270 shown in the following Table were synthesized using the methods described above such as Methods 1-15 and those set forth in the Schemes and other Examples or modified as apparent to one of reasonable skill in the art using commercially available materials.

Example	Name	LC/MS m/z (MH <sup>+</sup> )
155	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-chloro-6-iodoquinolin-2(1H)-one	547
156	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-nitroquinolin-2(1H)-one	431
157	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-methylquinolin-2(1H)-one	401
158	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6,7-difluoroquinolin-2(1H)-one	422
159	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-chloroquinolin-2(1H)-one	421
160	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-bromoquinolin-2(1H)-one	465
161	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-1,2-dihydroquinoline-6-carbonitrile	411
162	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoroquinolin-2(1H)-one	404
163	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6,7-bis(methoxy)quinolin-2(1H)-one	447
164	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6,7-dichloroquinolin-2(1H)-one	455
165	1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7-yl]piperidine-4-carboxamide	531
166	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-[(3-hydroxypropyl)amino]quinolin-2(1H)-one	478
167	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(dimethylamino)-6-fluoroquinolin-2(1H)-one	448
168	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoroquinolin-2(1H)-one	404

169	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-(4-nitrophenyl)quinolin-2(1H)-one	508
170	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-[[2-(dimethylamino)ethyl]amino]-6-fluoroquinolin-2(1H)-one	491
171	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-(1H-imidazol-1-yl)quinolin-2(1H)-one	471
172	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[4-(methyloxy)phenyl]quinolin-2(1H)-one	493
173	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-morpholin-4-ylquinolin-2(1H)-one	490
174	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6,7-difluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one	423
175	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-(3-nitrophenyl)quinolin-2(1H)-one	508
176	1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7-yl]piperidine-3-carboxamide	531
177	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-methylquinolin-2(1H)-one	401
178	6-(3-acetylphenyl)-4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one	506
179	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-chloroquinolin-2(1H)-one	421
180	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-fluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)-7-morpholin-4-ylquinolin-2(1H)-one	491
181	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(cyclopropylamino)-6-fluoroquinolin-2(1H)-one	460
182	N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-2-oxo-1,2-dihydroquinolin-6-yl]phenyl}acetamide	521



183	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-(4-methylpiperazin-1-yl)quinolin-2(1H)-one	503
184	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-fluoro-7-(1H-imidazol-1-yl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one	472
185	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-[(2-pyridin-2-ylethyl)amino]quinolin-2(1H)-one	525
186	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-piperidin-1-ylquinolin-2(1H)-one	488
187	6-chloro-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one	298
188	ethyl 1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7-yl]piperidine-4-carboxylate	560
189	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-(1-benzothien-2-yl)quinolin-2(1H)-one	519
190	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-pyrrolidin-1-ylquinolin-2(1H)-one	474
191	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-(trifluoromethyl)phenyl]quinolin-2(1H)-one	532
192	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-(methyloxy)phenyl]quinolin-2(1H)-one	494
193	ethyl 1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7-yl]piperidine-3-carboxylate	560
194	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-(4-ethylphenyl)quinolin-2(1H)-one	491
195	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-[(2-methylpropyl)amino]quinolin-2(1H)-one	476
196	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-methylquinolin-2(1H)-one	401
197	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-(2,4-dichlorophenyl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one	532

198	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[3-(trifluoromethyl)phenyl]quinolin-2(1H)-one	531
199	3-(1H-benzimidazol-2-yl)-4-(dimethylamino)quinolin-2(1H)-one	305
200	4-hydroxy-3-(1H-imidazo[4,5-f]quinolin-2-yl)quinolin-2(1H)-one	329
201	4-hydroxy-3-(1H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one	279
202	4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid	525
203	4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]benzamide	524
204	N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]phenyl}acetamide	538
205	3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid	525
206	4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid	525
207	N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]phenyl}acetamide	538
208	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-chloro-6-(2-methylphenyl)quinolin-2(1H)-one	511
209	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-1,2-dihydroquinoline-7-carbonitrile	411
210	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(methyloxy)quinolin-2(1H)-one	417
211	4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-1,2-dihydroquinolin-7-yl]benzamide	506
212	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-(methyloxy)quinolin-2(1H)-one	434
213	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-chloro-7-(dimethylamino)quinolin-2(1H)-one	464

214	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(dimethylamino)-6-iodoquinolin-2(1H)-one	555
215	3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(1H-imidazol-1-yl)-2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid	573
216	4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-7-piperidin-1-yl-1,2-dihydroquinolin-6-yl]benzoic acid	590
217	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(methyloxy)-6-[4-(methylsulfonyl)phenyl]quinolin-2(1H)-one	571
218	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-8-methylquinolin-2(1H)-one	401
219	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6,7-difluoroquinolin-2(1H)-one	422
220	3-(1H-benzimidazol-2-yl)-6-methyl-4-(piperidin-3-ylamino)quinolin-2(1H)-one	374
221	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[2-(methyloxy)phenyl]quinolin-2(1H)-one	493
222	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[3-(methyloxy)phenyl]quinolin-2(1H)-one	493
223	3-(1H-benzimidazol-2-yl)-6,7-difluoro-4-(piperidin-4-ylamino)quinolin-2(1H)-one	396
224	3-(1H-benzimidazol-2-yl)-6,7-difluoro-4-(pyrrolidin-3-ylamino)quinolin-2(1H)-one	382
225	3-(1H-benzimidazol-2-yl)-6-chloro-4-[(3-morpholin-4-ylpropyl)amino]quinolin-2(1H)-one	439
226	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-(piperidin-4-ylamino)quinolin-2(1H)-one	480
227	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(piperidin-2-ylmethyl)amino]quinolin-2(1H)-one	494
228	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	506

229	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-(piperidin-3-ylamino)quinolin-2(1H)-one	480
230	6-chloro-4-{{2-(dimethylamino)ethyl}amino}-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	468
231	4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	506
232	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(piperidin-3-ylmethyl)amino]quinolin-2(1H)-one	494
233	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(piperidin-4-ylmethyl)amino]quinolin-2(1H)-one	494
234	4-[(1R,2R)-2-aminocyclohexyl]amino-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	494
235	4-[(4-aminocyclohexyl)amino]-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	494
236	4-[(2S)-2-amino-3-methylbutyl]amino-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	482
237	4-[[4-(aminomethyl)phenyl]methyl]amino-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	516
238	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(pyrrolidin-2-ylmethyl)amino]quinolin-2(1H)-one	480
239	4-[(1R)-1-(aminomethyl)propyl]amino-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	468
240	4-[(1S)-2-amino-1-(phenylmethyl)ethyl]amino-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	530
241	6-chloro-4-{{3-(4-methylpiperazin-1-yl)propyl}amino}-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	537
242	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[[1-(phenylmethyl)piperidin-4-yl]amino]quinolin-2(1H)-one	570
243	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(3-morpholin-4-ylpropyl)amino]quinolin-2(1H)-one	524

244	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(2-piperidin-1-ylethyl)amino]quinolin-2(1H)-one	508
245	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(pyridin-3-ylmethyl)amino]quinolin-2(1H)-one	488
246	6-chloro-4-[[3-(1H-imidazol-1-yl)propyl]amino]-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	505
247	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(pyridin-4-ylmethyl)amino]quinolin-2(1H)-one	488
248	6-chloro-4-[[2-(methylamino)ethyl]amino]-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	454
249	6-chloro-4-[[2-(methyl-1-piperidin-4-yl-1H-benzimidazol-5-yl)methyl]amino]-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	624
250	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(2-pyrrolidin-1-ylethyl)amino]quinolin-2(1H)-one	494
251	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-(pyrrolidin-3-ylamino)quinolin-2(1H)-one	466
252	4-[[[(1R,2R)-2-aminocyclohexyl]amino]-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	507
253	4-[(4-aminocyclohexyl)amino]-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	507
254	4-[[4-(aminomethyl)phenyl]methyl]amino)-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	529
255	6-chloro-4-[[2-(methylamino)ethyl]amino]-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	467
256	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[[3-(4-methylpiperazin-1-yl)propyl]amino]quinolin-2(1H)-one	550
257	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[[1-(phenylmethyl)piperidin-4-yl]amino]quinolin-2(1H)-one	583

258	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(2-pyrrolidin-1-ylethyl)amino]quinolin-2(1H)-one	507
259	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-(pyrrolidin-3-ylamino)quinolin-2(1H)-one	479
260	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-(piperidin-4-ylamino)quinolin-2(1H)-one	493
261	6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(2-piperidin-2-ylethyl)amino]quinolin-2(1H)-one	508
262	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-7-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one	506
263	7-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-(piperidin-3-ylamino)quinolin-2(1H)-one	480
264	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(piperidin-2-ylmethyl)amino]quinolin-2(1H)-one	507
265	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(2S)-pyrrolidin-2-ylmethyl]amino]quinolin-2(1H)-one	493
266	6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(2R)-pyrrolidin-2-ylmethyl]amino]quinolin-2(1H)-one	493
267	6-chloro-4-({[(2S)-1-ethylpyrrolidin-2-yl]methyl}amino)-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	521
268	6-chloro-4-({[(2R)-1-ethylpyrrolidin-2-yl]methyl}amino)-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one	521
269	4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[4-(methyloxy)phenyl]quinolin-2(1H)-one	493
270	6-(3-aminophenyl)-4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)quinolin-2(1H)-one	478

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### Assay Procedures

#### **In vitro kinase assays for receptor tyrosine kinases**

The kinase activity of various protein tyrosine kinases can be measured by providing ATP and a suitable peptide or protein tyrosine-containing substrate, and assaying the transfer of phosphate moiety to the tyrosine residue. Recombinant proteins corresponding to the cytoplasmic domains of the flt-1 (VEGFR1), KDR (VEGFR2), and bFGF receptors were expressed in Sf9 insect cells using a Baculovirus expression system (InVitrogen) and purified via Glu antibody interaction (for Glu-epitope tagged constructs) or by Metal Ion Chromatography (for His<sub>6</sub> tagged constructs). For each assay, test compounds were serially diluted in DMSO then mixed with an appropriate kinase reaction buffer plus ATP. Kinase protein and an appropriate biotinylated peptide substrate were added to give a final volume of 100  $\mu$ L, reactions were incubated for 1-2 hours at room temperature and stopped by the addition of 50  $\mu$ L of 45 mM EDTA, 50 mM Hepes pH 7.5. Stopped reaction mix (75  $\mu$ L) was transferred to a streptavidin coated microtiter plate (Boehringer Mannheim) and incubated for 1 hour. Phosphorylated peptide product was measured with the DELFIA time-resolved fluorescence system (Wallac), using a Eu-labeled anti-phosphotyrosine antibody PT66 with the modification that the DELFIA assay buffer was supplemented with 1 mM MgCl<sub>2</sub> for the antibody dilution. Time resolved fluorescence was read on a Wallac 1232 DELFIA fluorometer. The concentration of each compound for 50% inhibition (IC<sub>50</sub>) was calculated by non-linear regression using XL Fit data analysis software.

Flt-1, KDR, and bFGFR kinases were assayed in 50 mM Hepes pH 7.0, 2 mM MgCl<sub>2</sub>, 10 mM MnCl<sub>2</sub>, 1 mM NaF, 1 mM DTT, 1 mg/ml BSA, 2  $\mu$ M ATP, and 0.42  $\mu$ M biotin-GGGGQDGKDYIVLPI-NH<sub>2</sub>. Flt-1, KDR, and bFGFR kinases were added at 0.1  $\mu$ g/mL, 0.05  $\mu$ g/mL, or 0.1  $\mu$ g/mL respectively.

Each of the following compounds was synthesized and assayed using the procedures described above:

- 3-{5-[2-(ethylanilino)ethoxy]-1H-benzimidazol-2-yl}-4-hydroxy-2(1H)-quinolinone;  
3-[5-(4-aminophenoxy)-1H-benzimidazol-2-yl]-4-hydroxy-2(1H)-quinolinone; 3-{6-  
5 [[2-(dimethylamino)ethyl](methyl)amino]-1H-benzimidazol-2-yl}-4-hydroxy-2(1H)-  
quinolinone; 4-hydroxy-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-  
quinolinone; 3-[5-(3-amino-1-pyrrolidinyl)-1H-benzimidazol-2-yl]-4-hydroxy-2(1H)-  
quinolinone; N,N-dimethyl-2-(2-oxo-1,2-dihydro-3-quinolinyl)-1H-benzimidazole-5-  
carboxamide; 3-{5-[2-(4-morpholinyl)ethoxy]-1H-benzimidazol-2-yl}-2(1H)-  
10 quinolinone; 3-{5-[3-(dimethylamino)-1-pyrrolidinyl]-1H-benzimidazol-2-yl}-2(1H)-  
quinolinone; 3-(1H-benzimidazol-2-yl)-2-oxo-1,2-dihydro-4-quinolinecarbonitrile; 4-  
amino-3-{5-[2-(4-morpholinyl)ethoxy]-1H-benzimidazol-2-yl}-2(1H)-quinolinone; 4-  
amino-3-[6-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-  
[6-(3-amino-1-pyrrolidinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 2-(4-amino-  
15 2-oxo-1,2-dihydro-3-quinolinyl)-1H-benzimidazole-5-carbonitrile; 2-(4-amino-2-  
oxo-1,2-dihydro-3-quinolinyl)-N,N-dimethyl-1H-benzimidazole-5-carboxamide; 4-  
amino-3-{5-[3-(dimethylamino)-1-pyrrolidinyl]-1H-benzimidazol-2-yl}-2(1H)-  
quinolinone; 2-(4-amino-2-oxo-1,2-dihydro-3-quinolinyl)-1H-benzimidazole-6-  
carboximidamide; 4-amino-3-[5-(4-morpholinylcarbonyl)-1H-benzimidazol-2-yl]-  
20 2(1H)-quinolinone; 4-amino-3-[5-(1H-1,2,4-triazol-1-yl)-1H-benzimidazol-2-yl]-  
2(1H)-quinolinone; 4-amino-3-[5-(dimethylamino)-1H-benzimidazol-2-yl]-2(1H)-  
quinolinone; 4-amino-3-[5-(1-piperidinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone;  
4-amino-3-[5-(2-thienyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-{5-  
[3-(1-pyrrolidinyl)propoxy]-1H-benzimidazol-2-yl}-2(1H)-quinolinone; 4-amino-3-  
25 {5-[3-(4-morpholinyl)propoxy]-1H-benzimidazol-2-yl}-2(1H)-quinolinone; 4-amino-  
3-[5-(3,5-dimethyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-  
amino-3-[5-(2,6-dimethyl-4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone;  
4-amino-3-[5-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-  
amino-3-(1H-benzimidazol-2-yl)-6-[hydroxy(oxido)amino]-2(1H)-quinolinone; 4-  
30 amino-3-(1H-benzimidazol-2-yl)-5-[2-(4-morpholinyl)ethoxy]-2(1H)-quinolinone; 4-



- amino-3-(1H-benzimidazol-2-yl)-6-(4-methyl-1-piperazinyl)-2(1H)-quinolinone; 4-amino-3-(1H-benzimidazol-2-yl)-5-[(1-methyl-3-piperidinyl)oxy]-2(1H)-quinolinone; 4-amino-6-chloro-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-6-chloro-3-{5-[3-(dimethylamino)-1-pyrrolidinyl]-1H-benzimidazol-2-yl}-2(1H)-quinolinone; 4-amino-6-[hydroxy(oxido)amino]-3-{5-[2-(4-morpholinyl)ethoxy]-1H-benzimidazol-2-yl}-2(1H)-quinolinone; 4-amino-5-[2-(4-morpholinyl)ethoxy]-3-{5-[2-(4-morpholinyl)ethoxy]-1H-benzimidazol-2-yl}-2(1H)-quinolinone; 4-amino-3-(1H-benzimidazol-2-yl)-6-(2-pyridinylmethoxy)-2(1H)-quinolinone; 4-amino-6-fluoro-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-amino-3-{5-[3-(dimethylamino)-1-pyrrolidinyl]-1H-benzimidazol-2-yl}-6-fluoro-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-[(tetrahydro-2-furanylmethyl)amino]-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-(methylamino)-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-(ethylamino)-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-{[2-(1-methyl-2-pyrrolidinyl)ethyl]amino}-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-[(4-piperidinylmethyl)amino]-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-(4-fluoroanilino)-2(1H)-quinolinone; 4-(1-azabicyclo[2.2.2]oct-3-ylamino)-3-(1H-benzimidazol-2-yl)-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-(1H-benzimidazol-6-ylamino)-2(1H)-quinolinone; 4-anilino-3-(1H-benzimidazol-2-yl)-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-(methoxyamino)-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-[(1H-imidazol-5-ylmethyl)amino]-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-(4-morpholinylamino)-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-hydrazino-2(1H)-quinolinone; 4-(1-azabicyclo[2.2.2]oct-3-ylamino)-3-(1H-benzimidazol-2-yl)-2(1H)-quinolinone; 4-(1-azabicyclo[2.2.2]oct-3-ylamino)-3-(1H-benzimidazol-2-yl)-2(1H)-quinolinone; 4-[(2-methoxyethyl)amino]-3-[6-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-[(2-hydroxyethyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-(methoxyamino)-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-(3-piperidinylamino)-2(1H)-quinolinone; 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[(3-piperidinylmethyl)amino]-2(1H)-quinolinone; 4-{2-

- (dimethylamino)ethyl]amino}-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-[(tetrahydro-2-furanylmethyl)amino]-2(1H)-quinolinone; 4-{[2-(methylamino)ethyl]amino}-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-4-(3-pyrrolidinylamino)-2(1H)-quinolinone; 4-[(2-amino-4-methylpentyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-[(2-amino-3-methylbutyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 3-(5,6-dimethyl-1H-benzimidazol-2-yl)-4-(3-piperidinylamino)-2(1H)-quinolinone; 4-[(2-aminocyclohexyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 4-[(2-aminocyclohexyl)amino]-3-[5-(4-morpholinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone; 3-(1H-benzimidazol-2-yl)-4-hydroxybenzo[g]quinolin-2(1H)-one; 4-amino-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-amino-3-(5-morpholin-4-yl-3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-amino-5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-3H-imidazo[4,5-b]pyridin-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-chloroquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-chloroquinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-4-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]quinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-6-chloro-4-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]quinolin-2(1H)-one; 4-amino-3-[5-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1-methylquinolin-2(1H)-one; 4-amino-3-(6-piperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-[6-(pyridin-4-ylmethyl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[(3R,5S)-3,5-dimethylpiperazin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-(6-methyl-5-morpholin-4-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[(1-methylpiperidin-3-yl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(2R,6S)-2,6-

dimethylmorpholin-4-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(1-methylpyrrolidin-3-yl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-[5-(4-methyl-1,4-diazepan-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-6-chloro-3-{5-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; ethyl {4-[2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-6-yl]piperazin-1-yl}acetate; 4-amino-3-{6-[methyl(1-methylpiperidin-4-yl)amino]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 3-[6-(4-acetylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-aminoquinolin-2(1H)-one; 4-amino-3-[6-(1,4'-bipiperidin-1'-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazole-6-carboxylic acid; 4-amino-5-(methoxy)-3-[6-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{6-[4-(1-methylethyl)piperazin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; {4-[2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-6-yl]piperazin-1-yl}acetic acid; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-[5-(4-ethylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[(2S,5S)-2-[(dimethylamino)methyl]-5-methylmorpholin-4-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-6-chloro-3-{5-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-5,6-dichloro-3-{5-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-5,6-dichloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-6-[(pyridin-2-ylmethyl)oxy]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-6-[(2R,6S)-2,6-dimethylmorpholin-4-yl]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-6-morpholin-4-ylquinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-5-[(1-methylpiperidin-3-yl)oxy]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-5-[(pyridin-2-ylmethyl)oxy]quinolin-2(1H)-one; 4-amino-3-

- (5-morpholin-4-yl-1H-benzimidazol-2-yl)-5-[(pyridin-4-ylmethyl)oxy]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-5-(methyloxy)quinolin-2(1H)-one; 4-amino-3-(5-methyl-1H-benzimidazol-2-yl)-5-(methyloxy)quinolin-2(1H)-one; 4-amino-3-{5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-1H-benzimidazol-2-yl}-5-(methyloxy)quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-5-morpholin-4-ylquinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-5-(4-methylpiperazin-1-yl)quinolin-2(1H)-one; 4-amino-5,6-dichloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 3-{5-[(2-morpholin-4-ylethyl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(3-pyrrolidin-1-ylpropyl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(3-morpholin-4-ylpropyl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-6-fluoro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}-6-fluoroquinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-6-fluoroquinolin-2(1H)-one; 4-amino-3-(6-fluoro-5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-{5-[(tetrahydrofuran-2-ylmethyl)oxy]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-6-fluoro-3-(6-fluoro-5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-[6-fluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-(5-{[2-(methyloxy)ethyl]oxy}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-[4,6-difluoro-5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}-5-fluoroquinolin-2(1H)-one; 4-amino-5-fluoro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-5-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-5-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-6-chloro-3-{5-[3-(dimethylamino)pyrrolidin-1-yl]-6-fluoro-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-3-(3H-imidazo[4,5-b]pyridin-2-

- yl)quinolin-2(1H)-one; 4-amino-3-(6-thiomorpholin-4-yl)-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-[5-(4-cyclohexylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{6-[3-(diethylamino)pyrrolidin-1-yl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-[6-(4-pyridin-2-ylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-[5-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one; 4-amino-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-imidazo[4,5-b]pyridin-2-yl]quinolin-2(1H)-one; 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N-methyl-N-(1-methylpiperidin-4-yl)-1H-benzimidazole-5-carboxamide; 4-amino-3-(5-{[4-(1-methylethyl)piperazin-1-yl]carbonyl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-6-nitroquinolin-2(1H)-one; 4-amino-3-[5-(1,4'-bipiperidin-1'-ylcarbonyl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-{5-[(4-methylpiperazin-1-yl)carbonyl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-[5-(1-oxidothiomorpholin-4-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 3-{5-[(4-acetylpiperazin-1-yl)carbonyl]-1H-benzimidazol-2-yl}-4-aminoquinolin-2(1H)-one; 4-amino-3-(5-{[(3R)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-(5-{[(3S)-3-(dimethylamino)pyrrolidin-1-yl]carbonyl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-amino-3-(5-{[4-(dimethylamino)piperidin-1-yl]carbonyl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; methyl 2-(4-amino-5-fluoro-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazole-6-carboxylate; 4-amino-3-[5-(1,3'-bipyrrolidin-1'-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-[5-(pyridin-3-yloxy)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-5,6-bis(methyloxy)-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N-[2-(dimethylamino)ethyl]-N-methyl-1H-benzimidazole-5-carboxamide; 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N-methyl-N-(1-methylpyrrolidin-3-yl)-1H-benzimidazole-5-carboxamide; 4-amino-3-{5-[(5-methyl-2,5-diazabicyclo[2.2.1]hept-2-yl)carbonyl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(4-cyclohexylpiperazin-1-yl)carbonyl]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(2-piperidin-1-ylethyl)amino]-1H-

benzimidazol-2-yl}quinolin-2(1H)-one; ethyl 4-{[2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-5-yl]amino}piperidine-1-carboxylate; 4-amino-3-[5-((5R)-5-[(methyloxy)methyl]pyrrolidin-3-yl)amino]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-{5-[(pyridin-2-ylmethyl)amino]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; 4-amino-3-[5-(piperidin-3-ylamino)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-5-fluoro-3-{5-[(pyridin-2-ylmethyl)amino]-1H-benzimidazol-2-yl}quinolin-2(1H)-one; ethyl 4-{[2-(4-amino-5-fluoro-2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazol-5-yl]amino}piperidine-1-carboxylate; 4-amino-5-fluoro-3-[5-(piperidin-3-ylamino)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-6-bromoquinolin-2(1H)-one; 4-amino-3-(1H-benzimidazol-2-yl)-7-bromoquinolin-2(1H)-one; 4-amino-3-(5-bromo-1H-benzimidazol-2-yl)quinolin-2(1H)-one; N,N-dimethyl-2-(2-oxo-1,2-dihydroquinolin-3-yl)-1H-benzimidazole-5-carboxamide; 4-amino-3-(5-thien-2-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 2-(4-amino-2-oxo-1,2-dihydroquinolin-3-yl)-N,N-dimethyl-1H-benzimidazole-5-sulfonamide; 4-amino-6-iodo-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-amino-3-(5-{2-[(dimethylamino)methyl]morpholin-4-yl}-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-chloro-6-iodoquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-nitroquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-methylquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6,7-difluoroquinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-chloroquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-bromoquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-1,2-dihydroquinoline-6-carbonitrile; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoroquinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6,7-bis(methyloxy)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6,7-dichloroquinolin-2(1H)-one; 1-[4-[(3S)-1-

- azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7-yl]piperidine-4-carboxamide; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-[(3-hydroxypropyl)amino]quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-
- 5 (dimethylamino)-6-fluoroquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoroquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-(4-nitrophenyl)quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-{[2-(dimethylamino)ethyl]amino}-6-fluoroquinolin-2(1H)-one;
- 10 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-(1H-imidazol-1-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[4-(methyloxy)phenyl]quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-morpholin-4-ylquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6,7-difluoro-3-
- 15 (3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-(3-nitrophenyl)quinolin-2(1H)-one; 1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7-yl]piperidine-3-carboxamide; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-methylquinolin-2(1H)-one; 6-(3-
- 20 acetylphenyl)-4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-chloroquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-fluoro-3-(3H-imidazo[4,5-b]pyridin-2-yl)-7-morpholin-4-ylquinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-
- 25 (cyclopropylamino)-6-fluoroquinolin-2(1H)-one; N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-2-oxo-1,2-dihydroquinolin-6-yl]phenyl}acetamide; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-(4-methylpiperazin-1-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-fluoro-7-(1H-imidazol-1-yl)-3-(3H-
- 30 imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-

- ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-[(2-pyridin-2-ylethyl)amino]quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-piperidin-1-ylquinolin-2(1H)-one; 6-chloro-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; ethyl 1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7-yl]piperidine-4-carboxylate; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-(1-benzothien-2-yl)quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-pyrrolidin-1-ylquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-(trifluoromethyl)phenyl]quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(3H-imidazo[4,5-b]pyridin-2-yl)-6-[2-(methyloxy)phenyl]quinolin-2(1H)-one; ethyl 1-[4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-2-oxo-1,2-dihydroquinolin-7-yl]piperidine-3-carboxylate; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-(4-ethylphenyl)quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-[(2-methylpropyl)amino]quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-methylquinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-(2,4-dichlorophenyl)-3-(3H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[3-(trifluoromethyl)phenyl]quinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-4-(dimethylamino)quinolin-2(1H)-one; 4-hydroxy-3-(1H-imidazo[4,5-f]quinolin-2-yl)quinolin-2(1H)-one; 4-hydroxy-3-(1H-imidazo[4,5-b]pyridin-2-yl)quinolin-2(1H)-one; 4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid; 4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]benzamide; N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]phenyl}acetamide; 3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-5-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid; 4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-fluoro-2-oxo-



- 1,2-dihydroquinolin-6-yl]benzoic acid; N-{3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-fluoro-2-oxo-1,2-dihydroquinolin-6-yl]phenyl}acetamide; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-chloro-6-(2-methylphenyl)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-1,2-dihydroquinoline-7-carbonitrile; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(methyloxy)quinolin-2(1H)-one; 4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-1,2-dihydroquinolin-7-yl]benzamide; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-fluoro-7-(methyloxy)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-chloro-7-(dimethylamino)quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(dimethylamino)-6-iodoquinolin-2(1H)-one; 3-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(1H-imidazol-1-yl)-2-oxo-1,2-dihydroquinolin-6-yl]benzoic acid; 4-[4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-2-oxo-7-piperidin-1-yl-1,2-dihydroquinolin-6-yl]benzoic acid; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-7-(methyloxy)-6-[4-(methylsulfonyl)phenyl]quinolin-2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-8-methylquinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6,7-difluoroquinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-6-methyl-4-(piperidin-3-ylamino)quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[2-(methyloxy)phenyl]quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[3-(methyloxy)phenyl]quinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-6,7-difluoro-4-(piperidin-4-ylamino)quinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-6,7-difluoro-4-(pyrrolidin-3-ylamino)quinolin-2(1H)-one; 3-(1H-benzimidazol-2-yl)-6-chloro-4-[(3-morpholin-4-ylpropyl)amino]quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-(piperidin-4-ylamino)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(piperidin-2-ylmethyl)amino]quinolin-

- 2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-(piperidin-3-ylamino)quinolin-2(1H)-one; 6-chloro-4-{2-(dimethylamino)ethyl}amino}-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-
- 5 2(1H)-one; 4-[(3R)-1-azabicyclo[2.2.2]oct-3-ylamino]-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(piperidin-3-ylmethyl)amino]quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(piperidin-4-ylmethyl)amino]quinolin-2(1H)-one; 4-{[(1R,2R)-2-aminocyclohexyl]amino}-6-chloro-3-(5-morpholin-4-yl-
- 10 1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-[(4-aminocyclohexyl)amino]-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-{[(2S)-2-amino-3-methylbutyl]amino}-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-{[4-(aminomethyl)phenyl]methyl}amino}-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-
- 15 benzimidazol-2-yl)-4-[(pyrrolidin-2-ylmethyl)amino]quinolin-2(1H)-one; 4-{[(1R)-1-(aminomethyl)propyl]amino}-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 4-{[(1S)-2-amino-1-(phenylmethyl)ethyl]amino}-6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-4-{[3-(4-methylpiperazin-1-yl)propyl]amino}-3-(5-morpholin-4-yl-1H-benzimidazol-2-
- 20 yl)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-{[1-(phenylmethyl)piperidin-4-yl]amino}quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(3-morpholin-4-ylpropyl)amino]quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(2-piperidin-1-ylethyl)amino]quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-
- 25 2-yl)-4-[(pyridin-3-ylmethyl)amino]quinolin-2(1H)-one; 6-chloro-4-{[3-(1H-imidazol-1-yl)propyl]amino}-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(pyridin-4-ylmethyl)amino]quinolin-2(1H)-one; 6-chloro-4-{[2-(methylamino)ethyl]amino}-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-4-{[(2-
- 30 methyl-1-piperidin-4-yl-1H-benzimidazol-5-yl)methyl]amino}-3-(5-morpholin-4-yl-

- 1H-benzimidazol-2-yl)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(2-pyrrolidin-1-ylethyl)amino]quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-(pyrrolidin-3-ylamino)quinolin-2(1H)-one; 4-[[[(1R,2R)-2-aminocyclohexyl]amino]-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-[(4-aminocyclohexyl)amino]-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-[[4-(aminomethyl)phenyl]methyl]amino)-6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 6-chloro-4-{[2-(methylamino)ethyl]amino}-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[[3-(4-methylpiperazin-1-yl)propyl]amino]quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[[1-(phenylmethyl)piperidin-4-yl]amino]quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(2-pyrrolidin-1-ylethyl)amino]quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-(pyrrolidin-3-ylamino)quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-(piperidin-4-ylamino)quinolin-2(1H)-one; 6-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-[(2-piperidin-2-ylethyl)amino]quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-7-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)quinolin-2(1H)-one; 7-chloro-3-(5-morpholin-4-yl-1H-benzimidazol-2-yl)-4-(piperidin-3-ylamino)quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(piperidin-2-ylmethyl)amino]quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[[[(2S)-pyrrolidin-2-ylmethyl]amino]quinolin-2(1H)-one; 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[[[(2R)-pyrrolidin-2-ylmethyl]amino]quinolin-2(1H)-one; 6-chloro-4-[[[(2S)-1-ethylpyrrolidin-2-yl]methyl]amino]-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 6-chloro-4-[[[(2R)-1-ethylpyrrolidin-2-yl]methyl]amino]-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]quinolin-2(1H)-one; 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)-6-[4-

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(methoxy)phenyl]quinolin-2(1H)-one; and 6-(3-aminophenyl)-4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1H-benzimidazol-2-yl)quinolin-2(1H)-one.

Each of the above compounds displayed an  $IC_{50}$  value of less than 10  $\mu$ M with respect to VEGFR1, VEGFR2, and bFGF.

5           It should be understood that the organic compounds according to the invention may exhibit the phenomenon of tautomerism. As the chemical structures within this specification can only represent one of the possible tautomeric forms, it should be understood that the invention encompasses any tautomeric form of the drawn structure.

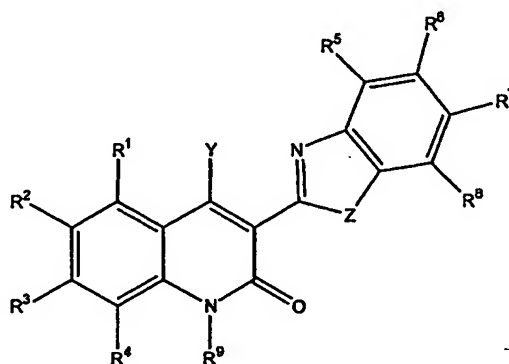
10           It is understood that the invention is not limited to the embodiments set forth herein for illustration, but embraces all such forms thereof as come within the scope of the following claims.

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## CLAIMS

What is claimed is:

- 1                    1.     A medicament, comprising: an anti-cancer drug selected from  
 2     5-FU or CPT 11 and a compound of formula I, a tautomer of the compound, a  
 3     pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable  
 4     salt of the tautomer



I

wherein,

- 7                    Y is selected from the group consisting of  $-OR^{10}$   
 8     groups,  $-C(=O)-R^{11}$  groups,  $-NR^{12}R^{13}$  groups, substituted and  
 9     unsubstituted alkynyl groups, substituted and unsubstituted  
 10     heterocyclalkyl groups, substituted and unsubstituted  
 11     alkylaminoalkyl groups, substituted and unsubstituted  
 12     dialkylaminoalkyl groups, substituted and unsubstituted  
 13     arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
 14     groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
 15     substituted and unsubstituted heterocyclaminoalkyl groups,  
 16     substituted and unsubstituted saturated heterocycl groups,  
 17     substituted and unsubstituted heterocycloxyalkyl groups, substituted

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18 and unsubstituted hydroxyalkyl groups, and substituted and  
19 unsubstituted aryloxyalkyl groups;

20 Z is selected from the group consisting of O, S, and  
21  $\text{NR}^{14}$  groups;

22  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , and  $\text{R}^4$  may be the same or different and  
23 are independently selected from the group consisting of H, Cl, Br, F,  
24 I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted and  
25 unsubstituted amidinyl groups, substituted and unsubstituted  
26 guanidinyl groups, substituted and unsubstituted primary, secondary,  
27 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
28 substituted and unsubstituted alkenyl groups, substituted and  
29 unsubstituted alkynyl groups, substituted and unsubstituted  
30 heterocyclyl groups, substituted and unsubstituted aminoalkyl groups,  
31 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
32 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
33 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
34 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
35 substituted and unsubstituted heterocyclylalkyl groups, substituted and  
36 unsubstituted diheterocyclylaminoalkyl groups, substituted and  
37 unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted and  
38 unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, and -C(=O)R<sup>18</sup>  
39 groups;

40  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ , and  $\text{R}^8$  may be the same or different and  
41 are independently selected from the group consisting of H, Cl, Br, F,  
42 I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups,  
43 -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted and  
44 unsubstituted amidinyl groups, substituted and unsubstituted

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45           guanidinyl groups, substituted and unsubstituted primary, secondary,  
46           and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
47           substituted and unsubstituted alkenyl groups, substituted and  
48           unsubstituted alkynyl groups, substituted and unsubstituted  
49           heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl  
50           groups,  $-C(=O)R^{25}$  groups, substituted and unsubstituted aminoalkyl  
51           groups, substituted and unsubstituted alkylaminoalkyl groups,  
52           substituted and unsubstituted dialkylaminoalkyl groups, substituted  
53           and unsubstituted arylaminoalkyl groups, substituted and  
54           unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
55           (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
56           heterocyclylaminoalkyl groups, substituted and unsubstituted  
57           diheterocyclylaminoalkyl groups, substituted and unsubstituted  
58           (heterocyclyl)(alkyl)aminoalkyl groups, substituted and unsubstituted  
59           (heterocyclyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
60           hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
61           groups, substituted and unsubstituted aryloxyalkyl groups, and  
62           substituted and unsubstituted heterocyclyloxyalkyl groups;

63                        $R^9$  and  $R^{14}$  may be the same or different and are  
64           independently selected from the group consisting of H, -OH,  
65           substituted and unsubstituted alkoxy groups, substituted and  
66           unsubstituted aryloxy groups,  $-NH_2$ , substituted and unsubstituted  
67           alkylamino groups, substituted and unsubstituted arylamino groups,  
68           substituted and unsubstituted dialkylamino groups, substituted and  
69           unsubstituted diarylamino groups, substituted and unsubstituted  
70           (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
71           substituted and unsubstituted aryl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl  
72           groups, and  $-C(=O)$ -aryl groups;

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73  $R^{10}$  is selected from the group consisting of substituted  
74 and unsubstituted aryl groups, substituted and unsubstituted  
75 heterocyclyl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl groups,  $-C(=O)$ -aryl  
76 groups,  $-C(=O)O$ -alkyl groups,  $-C(=O)O$ -aryl groups,  $-C(=O)NH_2$ ,  
77  $-C(=O)NH$ (alkyl) groups,  $-C(=O)NH$ (aryl) groups,  
78  $-C(=O)N$ (alkyl)<sub>2</sub> groups,  $-C(=O)N$ (aryl)<sub>2</sub> groups,  
79  $-C(=O)N$ (alkyl)(aryl) groups,  $-NH_2$ ,  $-NH$ (alkyl) groups,  $-NH$ (aryl)  
80 groups,  $-N$ (alkyl)<sub>2</sub> groups,  $-N$ (alkyl)(aryl) groups,  $-N$ (aryl)<sub>2</sub> groups,  
81  $-NH$ (heterocyclyl) groups,  $-N$ (heterocyclyl)<sub>2</sub> groups,  
82  $-N$ (alkyl)(heterocyclyl) groups,  $-N$ (aryl)(heterocyclyl),  
83  $-C(=O)NH$ (heterocyclyl) groups,  $-C(=O)N$ (heterocyclyl)<sub>2</sub> groups,  
84  $-C(=O)N$ (alkyl)(heterocyclyl) groups,  $-C(=O)N$ (aryl)(heterocyclyl)  
85 groups, and substituted and unsubstituted heterocyclylalkyl groups;

86  $R^{11}$  is selected from the group consisting of  $H$ ,  $-NH_2$ , -  
87  $NH$ (alkyl) groups,  $-NH$ (aryl) groups,  $-N$ (alkyl)<sub>2</sub> groups,  $-N$ (aryl)<sub>2</sub>  
88 groups,  $-N$ (alkyl)(aryl) groups,  $-NH$ (heterocyclyl) groups, -  
89  $N$ (heterocyclyl)<sub>2</sub> groups,  $-N$ (alkyl)(heterocyclyl) groups, -  
90  $N$ (aryl)(heterocyclyl) groups,  $-O$ -alkyl groups,  $O$ -aryl groups,  
91 heterocycloxyalkyl groups, and substituted and unsubstituted aryl  
92 groups;

93  $R^{12}$  is selected from the group consisting of  $H$ ,  
94 substituted and unsubstituted alkyl groups, substituted and  
95 unsubstituted aryl groups, and substituted and unsubstituted  
96 heterocyclyl groups;

97  $R^{13}$  is selected from the group consisting of substituted  
98 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
99 groups, substituted and unsubstituted heterocyclyl groups,  $-OH$ ,



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100 alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted and unsubstituted  
101 heterocyclalkyl groups, substituted and unsubstituted aminoalkyl  
102 groups, substituted and unsubstituted alkylaminoalkyl groups,  
103 substituted and unsubstituted dialkylaminoalkyl groups, substituted  
104 and unsubstituted arylaminoalkyl groups, substituted and  
105 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
106 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
107 alkylamino groups, substituted and unsubstituted arylamino groups,  
108 substituted and unsubstituted dialkylamino groups, substituted and  
109 unsubstituted diarylamino groups, substituted and unsubstituted  
110 (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-  
111 aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -  
112 C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,  
113 -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
114 -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocycl groups,  
115 -C(=O)-O-heterocycl groups, -C(=O)NH(heterocycl) groups,  
116 -C(=O)-N(heterocycl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocycl)  
117 groups, substituted and unsubstituted heterocyclaminoalkyl groups,  
118 substituted and unsubstituted hydroxyalkyl groups, substituted and  
119 unsubstituted alkoxyalkyl groups, substituted and unsubstituted  
120 aryloxyalkyl groups, substituted and unsubstituted  
121 heterocyclloxyalkyl groups, and -C(=O)-N(alkyl)(heterocycl)  
122 groups;

123 R<sup>15</sup> and R<sup>19</sup> may be the same or different and are  
124 independently selected from the group consisting of substituted and  
125 unsubstituted alkyl groups, substituted and unsubstituted aryl groups,  
126 substituted and unsubstituted heterocycl groups, substituted and  
127 unsubstituted heterocyclalkyl groups, -C(=O)H, -C(=O)-alkyl  
128 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)

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129 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -  
130 C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -  
131 NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -  
132 N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl) groups,  
133 substituted and unsubstituted aminoalkyl groups, substituted and  
134 unsubstituted alkylaminoalkyl groups, substituted and unsubstituted  
135 dialkylaminoalkyl groups, substituted and unsubstituted  
136 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
137 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
138 substituted and unsubstituted heterocyclylaminoalkyl, substituted and  
139 unsubstituted diheterocyclylaminoalkyl, substituted and unsubstituted  
140 (heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted  
141 (heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted  
142 alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl  
143 groups, substituted and unsubstituted aryloxyalkyl groups, and  
144 substituted and unsubstituted heterocyclyoxyalkyl groups;

145 R<sup>16</sup> and R<sup>20</sup> may be the same or different and are  
146 independently selected from the group consisting of H, substituted  
147 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
148 groups, and substituted and unsubstituted heterocyclyl groups;

149 R<sup>17</sup> and R<sup>21</sup> may be the same or different and are  
150 independently selected from the group consisting of H, substituted  
151 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
152 groups, substituted and unsubstituted heterocyclyl groups, -C(=O)H,  
153 -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -  
154 C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub>  
155 groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups,  
156 -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted and

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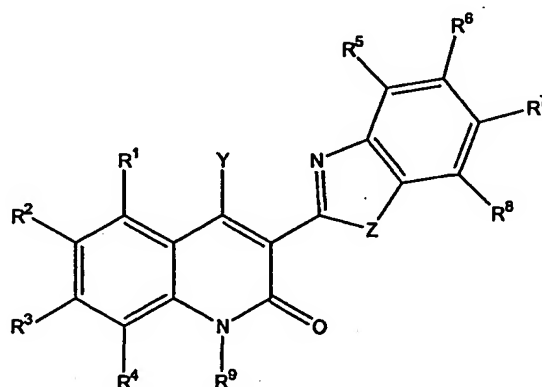
157 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted  
158 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
159 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
160 substituted and unsubstituted arylaminoalkyl groups, substituted and  
161 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
162 (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,  
163 -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
164 -C(=O)N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocyclyl)  
165 groups, substituted and unsubstituted heterocyclylaminoalkyl groups,  
166 substituted and unsubstituted diheterocyclylaminoalkyl groups,  
167 substituted and unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups,  
168 substituted and unsubstituted (heterocyclyl)(aryl)aminoalkyl groups,  
169 substituted and unsubstituted hydroxyalkyl groups, substituted and  
170 unsubstituted alkoxyalkyl groups, substituted and unsubstituted  
171 aryloxyalkyl groups, substituted and unsubstituted  
172 heterocycliloxyalkyl groups, and -C(=O)-N(alkyl)(heterocyclyl)  
173 groups;

174  $R^{18}$ ,  $R^{23}$ ,  $R^{24}$ , and  $R^{25}$  may be the same or different and  
175 are independently selected from the group consisting of H, -NH<sub>2</sub>,  
176 -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub>  
177 groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups,  
178 -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,  
179 -N(heterocyclyl)<sub>2</sub> groups, substituted and unsubstituted alkyl groups,  
180 substituted and unsubstituted aryl groups, -OH, substituted and  
181 unsubstituted alkoxy groups, substituted and unsubstituted  
182 heterocyclyl groups, substituted and unsubstituted aryloxy groups,  
183 heterocycliloxy groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH  
184 groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, -N(alkyl)O-  
185 aryl groups, and -N(aryl)O-aryl groups; and

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186  $R^{22}$  is selected from the group consisting of substituted  
 187 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
 188 groups, and substituted and unsubstituted heterocyclyl groups.

1 2. A medicament, comprising: an anti-cancer drug selected from  
 2 5-FU or CPT 11 and a compound of formula I, a tautomer of the compound, a  
 3 pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable  
 4 salt of the tautomer



I

wherein,

5  
 6  
 7 Y is selected from the group consisting of  $-OR^{10}$   
 8 groups,  $-C(=O)-R^{11}$  groups,  $-NR^{12}R^{13}$  groups, substituted and  
 9 unsubstituted alkynyl groups, substituted and unsubstituted  
 10 heterocyclalkyl groups, substituted and unsubstituted  
 11 alkylaminoalkyl groups, substituted and unsubstituted  
 12 dialkylaminoalkyl groups, substituted and unsubstituted  
 13 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
 14 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
 15 substituted and unsubstituted heterocyclaminoalkyl groups,  
 16 substituted and unsubstituted saturated heterocyclyl groups,  
 17 substituted and unsubstituted heterocycloxyalkyl groups, substituted

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18 and unsubstituted hydroxyalkyl groups, and substituted and  
19 unsubstituted aryloxyalkyl groups;

20 Z is selected from the group consisting of O, S, and  
21  $\text{NR}^{14}$  groups;

22  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , and  $\text{R}^4$  may be the same or different and  
23 are independently selected from the group consisting of H, Cl, Br, F,  
24 I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted and  
25 unsubstituted amidinyl groups, substituted and unsubstituted  
26 guanidinyl groups, substituted and unsubstituted primary, secondary,  
27 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
28 substituted and unsubstituted alkenyl groups, substituted and  
29 unsubstituted alkynyl groups, substituted and unsubstituted  
30 heterocyclyl groups, substituted and unsubstituted aminoalkyl groups,  
31 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
32 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
33 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
34 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
35 substituted and unsubstituted heterocyclylalkyl groups, and -  
36  $\text{C}(=\text{O})\text{R}^{18}$  groups;

37  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ , and  $\text{R}^8$  may be the same or different and  
38 are independently selected from the group consisting of H, Cl, Br, F,  
39 I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups,  
40 -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted and  
41 unsubstituted amidinyl groups, substituted and unsubstituted  
42 guanidinyl groups, substituted and unsubstituted primary, secondary,  
43 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
44 substituted and unsubstituted alkenyl groups, substituted and

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45 unsubstituted alkynyl groups, substituted and unsubstituted  
46 heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl  
47 groups,  $-C(=O)R^{25}$  groups, substituted and unsubstituted aminoalkyl  
48 groups, substituted and unsubstituted alkylaminoalkyl groups,  
49 substituted and unsubstituted dialkylaminoalkyl groups, substituted  
50 and unsubstituted arylaminoalkyl groups, substituted and  
51 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
52 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
53 heterocyclylaminoalkyl groups, substituted and unsubstituted  
54 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
55 groups, substituted and unsubstituted aryloxyalkyl groups, and  
56 substituted and unsubstituted heterocycloxyalkyl groups;

57  $R^9$  is selected from the group consisting of  $-OH$ ,  
58 substituted and unsubstituted alkoxy groups, substituted and  
59 unsubstituted aryloxy groups,  $-NH_2$ , substituted and unsubstituted  
60 alkylamino groups, substituted and unsubstituted arylamino groups,  
61 substituted and unsubstituted dialkylamino groups, substituted and  
62 unsubstituted diarylamino groups, substituted and unsubstituted  
63 (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
64 substituted and unsubstituted aryl groups,  $-C(=O)H$ ,  $-C(=O)-alkyl$   
65 groups, and  $-C(=O)-aryl$  groups;

66  $R^{10}$  is selected from the group consisting of substituted  
67 and unsubstituted aryl groups, substituted and unsubstituted  
68 heterocyclyl groups,  $-C(=O)H$ ,  $-C(=O)-alkyl$  groups,  $-C(=O)-aryl$   
69 groups,  $-C(=O)O-alkyl$  groups,  $-C(=O)O-aryl$  groups,  $-C(=O)NH_2$ ,  
70  $-C(=O)NH(alkyl)$  groups,  $-C(=O)NH(aryl)$  groups,  
71  $-C(=O)N(alkyl)_2$  groups,  $-C(=O)N(aryl)_2$  groups,  
72  $-C(=O)N(alkyl)(aryl)$  groups,  $-NH_2$ ,  $-NH(alkyl)$  groups,  $-NH(aryl)$

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73 groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups,  
74 -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups,  
75 -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl)  
76 groups, and substituted and unsubstituted heterocyclylalkyl groups;

77 R<sup>11</sup> is selected from the group consisting of H, -NH<sub>2</sub>, -  
78 NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub>  
79 groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -  
80 N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, -O-alkyl  
81 groups, O-aryl groups, substituted and unsubstituted alkyl groups,  
82 and substituted and unsubstituted aryl groups;

83 R<sup>12</sup> is selected from the group consisting of H,  
84 substituted and unsubstituted alkyl groups, substituted and  
85 unsubstituted aryl groups, and substituted and unsubstituted  
86 heterocyclyl groups;

87 R<sup>13</sup> is selected from the group consisting of H,  
88 substituted and unsubstituted alkyl groups, substituted and  
89 unsubstituted aryl groups, substituted and unsubstituted heterocyclyl  
90 groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted and  
91 unsubstituted alkylamino groups, substituted and unsubstituted  
92 arylamino groups, substituted and unsubstituted dialkylamino groups,  
93 substituted and unsubstituted diarylamino groups, substituted and  
94 unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl  
95 groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl  
96 groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)  
97 groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
98 -C(=O)N(alkyl)(aryl) groups, substituted and unsubstituted  
99 heterocyclylalkyl groups, substituted and unsubstituted aminoalkyl

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100 groups, substituted and unsubstituted alkylaminoalkyl groups,  
101 substituted and unsubstituted dialkylaminoalkyl groups, substituted  
102 and unsubstituted arylaminoalkyl groups, substituted and  
103 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
104 (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,  
105 -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
106 -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocyclyl)  
107 groups, -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and  
108 unsubstituted heterocyclylaminoalkyl groups, substituted and  
109 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
110 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
111 groups, and substituted and unsubstituted heterocycloxyalkyl  
112 groups;

113  $R^{14}$  is selected from the group consisting of H, -OH,  
114 substituted and unsubstituted alkoxy groups, substituted and  
115 unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted and unsubstituted  
116 alkylamino groups, substituted and unsubstituted arylamino groups,  
117 substituted and unsubstituted dialkylamino groups, substituted and  
118 unsubstituted diarylamino groups, substituted and unsubstituted  
119 (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
120 substituted and unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl  
121 groups, and -C(=O)-aryl groups;

122  $R^{15}$  and  $R^{19}$  may be the same or different and are  
123 independently selected from the group consisting of substituted and  
124 unsubstituted alkyl groups, substituted and unsubstituted aryl groups,  
125 substituted and unsubstituted heterocyclyl groups, substituted and  
126 unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl  
127 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)



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128 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -  
129 C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted  
130 and unsubstituted aminoalkyl groups, substituted and unsubstituted  
131 alkylaminoalkyl groups, substituted and unsubstituted  
132 dialkylaminoalkyl groups, substituted and unsubstituted  
133 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
134 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
135 substituted and unsubstituted heterocyclylaminoalkyl, substituted and  
136 unsubstituted diheterocyclylaminoalkyl, substituted and unsubstituted  
137 (heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted  
138 (heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted  
139 alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl  
140 groups, substituted and unsubstituted aryloxyalkyl groups, and  
141 substituted and unsubstituted heterocyclyloxyalkyl groups;

142 R<sup>16</sup> and R<sup>20</sup> may be the same or different and are  
143 independently selected from the group consisting of H, substituted  
144 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
145 groups, and substituted and unsubstituted heterocyclyl groups;

146 R<sup>17</sup> and R<sup>21</sup> may be the same or different and are  
147 independently selected from the group consisting of H, substituted  
148 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
149 groups, substituted and unsubstituted heterocyclyl groups, -C(=O)H,  
150 -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -  
151 C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub>  
152 groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups,  
153 -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted and  
154 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted  
155 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl

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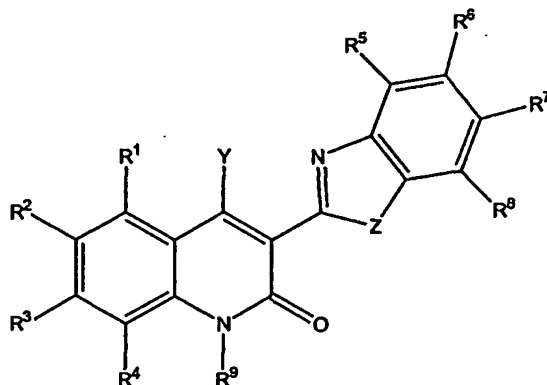
156 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
157 substituted and unsubstituted arylaminoalkyl groups, substituted and  
158 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
159 (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,  
160 -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
161 -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocyclyl)  
162 groups, -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and  
163 unsubstituted heterocyclylaminoalkyl groups, substituted and  
164 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
165 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
166 groups, and substituted and unsubstituted heterocycloxyalkyl  
167 groups;

168 R<sup>18</sup>, R<sup>23</sup>, R<sup>24</sup>, and R<sup>25</sup> may be the same or different and  
169 are independently selected from the group consisting of H, -NH<sub>2</sub>,  
170 -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub>  
171 groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups,  
172 -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,  
173 -N(heterocyclyl)<sub>2</sub> groups, substituted and unsubstituted alkyl groups,  
174 substituted and unsubstituted aryl groups, -OH, substituted and  
175 unsubstituted alkoxy groups, substituted and unsubstituted  
176 heterocyclyl groups, substituted and unsubstituted aryloxy groups,  
177 -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl  
178 groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, and  
179 -N(aryl)O-aryl groups; and

180 R<sup>22</sup> is selected from the group consisting of substituted  
181 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
182 groups, and substituted and unsubstituted heterocyclyl groups.

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- 1                    3.     A medicament, comprising: an anti-cancer drug selected from  
 2     5-FU or CPT 11 and a compound of formula I, a tautomer of the compound, a  
 3     pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable  
 4     salt of the tautomer



I

wherein,

- 5  
 6  
 7                    Y is selected from the group consisting of -OH, SH,  
 8     alkylthio groups, arylthio groups, -OR<sup>10</sup> groups, -C(=O)-R<sup>11</sup> groups,  
 9     -NR<sup>12</sup>R<sup>13</sup> groups, -CN, substituted and unsubstituted alkyl groups,  
 10     substituted and unsubstituted alkenyl groups, substituted and  
 11     unsubstituted alkynyl groups, substituted and unsubstituted aralkyl  
 12     groups, substituted and unsubstituted heterocyclalkyl groups,  
 13     substituted and unsubstituted alkylaminoalkyl groups, substituted and  
 14     unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
 15     arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
 16     groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
 17     substituted and unsubstituted heterocyclaminoalkyl groups,  
 18     substituted and unsubstituted heterocycl groups, substituted and  
 19     unsubstituted aryl groups, substituted and unsubstituted  
 20     heterocycloxyalkyl groups, substituted and unsubstituted

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21 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
22 groups, and substituted and unsubstituted aryloxyalkyl groups;

23 Z is selected from the group consisting of O, S, and  
24  $\text{NR}^{14}$  groups;

25  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , and  $\text{R}^4$  may be the same or different and  
26 are independently selected from the group consisting of H, Cl, Br, F,  
27 I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted and  
28 unsubstituted amidinyl groups, substituted and unsubstituted  
29 guanidinyl groups, substituted and unsubstituted primary, secondary,  
30 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
31 substituted and unsubstituted alkenyl groups, substituted and  
32 unsubstituted alkynyl groups, substituted and unsubstituted  
33 heterocyclyl groups, substituted and unsubstituted aminoalkyl groups,  
34 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
35 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
36 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
37 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
38 substituted and unsubstituted heterocyclylalkyl groups, and -  
39  $\text{C}(=\text{O})\text{R}^{18}$  groups;

40  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ , and  $\text{R}^8$  may be the same or different and  
41 are independently selected from the group consisting of H, Cl, Br, F,  
42 I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups,  
43 -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted and  
44 unsubstituted amidinyl groups, substituted and unsubstituted  
45 guanidinyl groups, substituted and unsubstituted primary, secondary,  
46 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
47 substituted and unsubstituted alkenyl groups, substituted and

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48 unsubstituted alkynyl groups, substituted and unsubstituted  
49 heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl  
50 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
51 substituted and unsubstituted arylaminoalkyl groups, substituted and  
52 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
53 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
54 heterocyclylalkyl groups,  $-C(=O)R^{25}$  groups, substituted and  
55 unsubstituted aminoalkyl groups, substituted and unsubstituted  
56 heterocyclylaminoalkyl groups, substituted and unsubstituted  
57 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
58 groups, substituted and unsubstituted aryloxyalkyl groups, and  
59 substituted and unsubstituted heterocycloxyalkyl groups;

60  $R^9$  and  $R^{14}$  may be the same or different and are  
61 independently selected from the group consisting of H, -OH,  
62 substituted and unsubstituted alkoxy groups, substituted and  
63 unsubstituted aryloxy groups,  $-NH_2$ , substituted and unsubstituted  
64 alkylamino groups, substituted and unsubstituted arylamino groups,  
65 substituted and unsubstituted dialkylamino groups, substituted and  
66 unsubstituted diarylamino groups, substituted and unsubstituted  
67 (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
68 substituted and unsubstituted aryl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl  
69 groups, and  $-C(=O)$ -aryl groups;

70  $R^{10}$  is selected from the group consisting of substituted  
71 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
72 groups, substituted and unsubstituted heterocyclyl groups, substituted  
73 and unsubstituted heterocyclylalkyl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl  
74 groups,  $-C(=O)$ -aryl groups,  $-C(=O)O$ -alkyl groups,  $-C(=O)O$ -aryl  
75 groups,  $-C(=O)NH_2$ ,  $-C(=O)NH$ (alkyl) groups,  $-C(=O)NH$ (aryl)

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76 groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
77 -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
78 groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups,  
79 -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups,  
80 -C(=O)N(alkyl)(heterocyclyl) groups, and  
81 -C(=O)N(aryl)(heterocyclyl) groups;

82 R<sup>11</sup> is selected from the group consisting of H, -OH,  
83 alkoxy groups, aryloxy groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
84 groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups,  
85 substituted and unsubstituted alkyl groups, -NH(heterocyclyl) groups,  
86 -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, and  
87 substituted and unsubstituted aryl groups;

88 R<sup>12</sup> is selected from the group consisting of H,  
89 substituted and unsubstituted alkyl groups, substituted and  
90 unsubstituted aryl groups, and substituted and unsubstituted  
91 heterocyclyl groups;

92 R<sup>13</sup> is selected from the group consisting of H,  
93 substituted and unsubstituted alkyl groups, substituted and  
94 unsubstituted aryl groups, substituted and unsubstituted heterocyclyl  
95 groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted and  
96 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted  
97 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
98 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
99 substituted and unsubstituted arylaminoalkyl groups, substituted and  
100 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
101 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
102 alkylamino groups, substituted and unsubstituted arylamino groups,

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103 substituted and unsubstituted dialkylamino groups, substituted and  
104 unsubstituted diarylamino groups, substituted and unsubstituted  
105 (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-  
106 aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -  
107 C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,  
108 -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
109 -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups,  
110 -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
111 -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocyclyl)  
112 groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and  
113 unsubstituted heterocyclylaminoalkyl groups, substituted and  
114 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
115 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
116 groups, and substituted and unsubstituted heterocycloxyalkyl  
117 groups;

118 R<sup>15</sup> and R<sup>19</sup> may be the same or different and are  
119 independently selected from the group consisting of substituted and  
120 unsubstituted alkyl groups, substituted and unsubstituted aryl groups,  
121 substituted and unsubstituted heterocyclyl groups, substituted and  
122 unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl  
123 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)  
124 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -  
125 C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted  
126 and unsubstituted aminoalkyl groups, substituted and unsubstituted  
127 alkylaminoalkyl groups, substituted and unsubstituted  
128 dialkylaminoalkyl groups, substituted and unsubstituted  
129 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
130 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
131 substituted and unsubstituted heterocyclylaminoalkyl, substituted and

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132 unsubstituted diheterocyclylaminoalkyl, substituted and unsubstituted  
133 (heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted  
134 (heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted  
135 alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl  
136 groups, substituted and unsubstituted aryloxyalkyl groups, and  
137 substituted and unsubstituted heterocycloxyalkyl groups;

138  $R^{16}$  and  $R^{20}$  may be the same or different and are  
139 independently selected from the group consisting of H, substituted  
140 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
141 groups, and substituted and unsubstituted heterocyclyl groups;

142  $R^{17}$  and  $R^{21}$  may be the same or different and are  
143 independently selected from the group consisting of H, substituted  
144 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
145 groups, substituted and unsubstituted heterocyclyl groups,  $-C(=O)H$ ,  
146  $-C(=O)$ -alkyl groups,  $-C(=O)$ -aryl groups,  $-C(=O)NH_2$ , -  
147  $C(=O)NH(alkyl)$  groups,  $-C(=O)NH(aryl)$  groups,  $-C(=O)N(alkyl)_2$   
148 groups,  $-C(=O)N(aryl)_2$  groups,  $-C(=O)N(alkyl)(aryl)$  groups,  
149  $-C(=O)O$ -alkyl groups,  $-C(=O)O$ -aryl groups, substituted and  
150 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted  
151 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
152 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
153 substituted and unsubstituted arylaminoalkyl groups, substituted and  
154 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
155 (alkyl)(aryl)aminoalkyl groups,  $-C(=O)$ -heterocyclyl groups,  
156  $-C(=O)-O$ -heterocyclyl groups,  $-C(=O)NH(heterocyclyl)$  groups,  
157  $-C(=O)-N(heterocyclyl)_2$  groups,  $-C(=O)-N(alkyl)(heterocyclyl)$   
158 groups,  $-C(=O)-N(aryl)(heterocyclyl)$  groups, substituted and  
159 unsubstituted heterocyclylaminoalkyl groups, substituted and



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160 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
161 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
162 groups, and substituted and unsubstituted heterocycloxyalkyl  
163 groups;

164  $R^{18}$ ,  $R^{23}$ ,  $R^{24}$ , and  $R^{25}$  may be the same or different and  
165 are independently selected from the group consisting of H,  $-NH_2$ ,  
166  $-NH(alkyl)$  groups,  $-NH(aryl)$  groups,  $-N(alkyl)_2$  groups,  $-N(aryl)_2$   
167 groups,  $-N(alkyl)(aryl)$  groups,  $-NH(heterocyclyl)$  groups,  
168  $-N(heterocyclyl)(alkyl)$  groups,  $-N(heterocyclyl)(aryl)$  groups,  
169  $-N(heterocyclyl)_2$  groups, substituted and unsubstituted alkyl groups,  
170 substituted and unsubstituted aryl groups,  $-OH$ , substituted and  
171 unsubstituted alkoxy groups, substituted and unsubstituted aryloxy  
172 groups, substituted and unsubstituted heterocyclyl groups,  $-NHOH$ ,  
173  $-N(alkyl)OH$  groups,  $-N(aryl)OH$  groups,  $-N(alkyl)O-alkyl$  groups,  
174  $-N(aryl)O-alkyl$  groups,  $-N(alkyl)O-aryl$  groups, and  $-N(aryl)O-aryl$   
175 groups; and

176  $R^{22}$  is selected from the group consisting of substituted  
177 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
178 groups, and substituted and unsubstituted heterocyclyl groups;

179 and further wherein at least one of  $R^5$ ,  $R^6$ ,  $R^7$ , or  $R^8$  is  
180 selected from the group consisting of substituted and unsubstituted  
181 amidinyl groups, substituted and unsubstituted guanidinyl groups,  
182 substituted and unsubstituted saturated heterocyclyl groups,  
183 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
184 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
185 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
186 groups, substituted and unsubstituted  $(alkyl)(aryl)aminoalkyl$  groups,

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187 substituted and unsubstituted heterocyclylalkyl groups, substituted and  
188 unsubstituted heterocyclylaminoalkyl groups, substituted and  
189 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
190 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
191 groups, and substituted and unsubstituted heterocyclyloxyalkyl  
192 groups;  $-OR^{19}$  groups wherein  $R^{19}$  is selected from the group  
193 consisting of substituted and unsubstituted aryl groups, substituted  
194 and unsubstituted heterocyclyl groups, substituted and unsubstituted  
195 heterocyclylalkyl groups,  $-C(=O)H$ ,  $-C(=O)$ -aryl groups,  
196  $-C(=O)NH_2$ ,  $-C(=O)NH(alkyl)$  groups,  $-C(=O)NH(aryl)$  groups,  
197  $-C(=O)N(alkyl)_2$  groups,  $-C(=O)N(aryl)_2$  groups,  
198  $-C(=O)N(alkyl)(aryl)$  groups, substituted and unsubstituted  
199 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
200 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
201 substituted and unsubstituted arylaminoalkyl groups, substituted and  
202 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
203  $(alkyl)(aryl)$ aminoalkyl groups, substituted and unsubstituted  
204 heterocyclylaminoalkyl groups, substituted and unsubstituted  
205 diheterocyclylaminoalkyl groups, substituted and unsubstituted  
206  $(heterocyclyl)(alkyl)$ aminoalkyl groups, substituted and unsubstituted  
207  $(heterocyclyl)(aryl)$ aminoalkyl groups, substituted and unsubstituted  
208 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
209 groups, substituted and unsubstituted aryloxyalkyl groups, and  
210 substituted and unsubstituted heterocyclyloxyalkyl groups;  $-NR^{20}R^{21}$   
211 groups wherein  $R^{20}$  is selected from the group consisting of  
212 substituted and unsubstituted heterocyclyl groups;  $-NR^{20}R^{21}$  groups  
213 wherein  $R^{21}$  is selected from the group consisting of substituted and  
214 unsubstituted heterocyclyl groups,  $-C(=O)H$ ,  $-C(=O)$ -aryl groups,  
215  $-C(=O)NH_2$ ,  $-C(=O)NH(alkyl)$  groups,  $-C(=O)NH(aryl)$  groups,  
216  $-C(=O)N(alkyl)_2$  groups,  $-C(=O)N(aryl)_2$  groups,

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217 -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl  
218 groups, substituted and unsubstituted aminoalkyl groups, substituted  
219 and unsubstituted alkylaminoalkyl groups, substituted and  
220 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
221 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
222 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
223 substituted and unsubstituted heterocyclylaminoalkyl groups,  
224 substituted and unsubstituted hydroxyalkyl groups, substituted and  
225 unsubstituted alkoxyalkyl groups, substituted and unsubstituted  
226 aryloxyalkyl groups, substituted and unsubstituted heterocyclylalkyl  
227 groups, and substituted and unsubstituted heterocyclyloxyalkyl  
228 groups; and -C(=O)R<sup>25</sup> groups wherein R<sup>25</sup> is selected from the  
229 group consisting of H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -  
230 N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -  
231 NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -  
232 N(heterocyclyl)(aryl) groups, -N(heterocyclyl)<sub>2</sub> groups, substituted  
233 and unsubstituted aryl groups, substituted and unsubstituted aryloxy  
234 groups, and substituted and unsubstituted heterocyclyl groups.

1 4. The medicament according to claim 3, wherein Y is selected  
2 from the group consisting of -OR<sup>10</sup> groups, -NR<sup>12</sup>R<sup>13</sup> groups, and substituted and  
3 unsubstituted alkynyl groups.

1 5. The medicament according to claim 3, wherein Z is an -NR<sup>14</sup>  
2 group.

1 6. The medicament according to claim 3, wherein R<sup>1</sup> is selected  
2 from the group consisting of -H, substituted and unsubstituted alkoxy groups,  
3 substituted and unsubstituted heterocyclylalkoxy groups, substituted and  
4 unsubstituted heterocyclyloxy groups, and substituted and unsubstituted heterocyclyl  
5 groups.

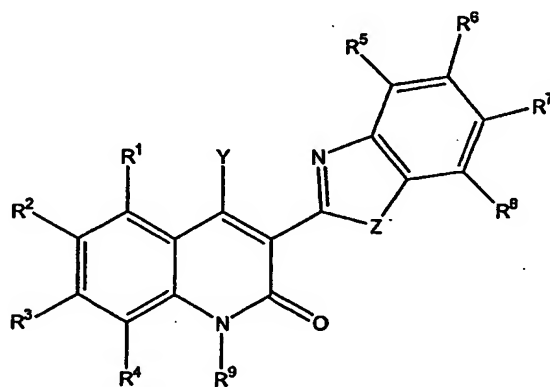
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1                    7.     The medicament according to claim 3, wherein  $R^2$  is selected  
 2     from the group consisting of H, F, Cl,  $-NO_2$ , substituted and unsubstituted  
 3     heterocyclyl groups, and substituted and unsubstituted heterocyclalkoxy groups.

1                    8.     The medicament according to claim 3, wherein  $R^6$  or  $R^7$  is an  
 2     alkyl group.

1                    9.     The medicament according to claim 3, wherein  $R^6$  or  $R^7$  is an  
 2      $-OR^{19}$  group and  $R^{19}$  is an alkyl group, an aryl group, a heterocyclyl group, or a  
 3     heterocyclalkyl group.

1                    10.    A medicament, comprising: an anti-cancer drug selected from  
 2     5-FU or CPT 11 and a compound of formula I, a tautomer of the compound, a  
 3     pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable  
 4     salt of the tautomer



I

wherein,

7                    Y is selected from the group consisting of  $-OH$ ,  $SH$ ,  
 8     alkylthio groups, arylthio groups,  $-OR^{10}$  groups,  $-C(=O)-R^{11}$  groups,  
 9      $-NR^{12}R^{13}$  groups,  $-CN$ , substituted and unsubstituted alkyl groups,  
 10     substituted and unsubstituted alkenyl groups, substituted and

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11 unsubstituted alkynyl groups, substituted and unsubstituted aralkyl  
12 groups, substituted and unsubstituted heterocyclalkyl groups,  
13 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
14 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
15 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
16 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
17 substituted and unsubstituted heterocyclalkylaminoalkyl groups,  
18 substituted and unsubstituted heterocycl groups, substituted and  
19 unsubstituted aryl groups, substituted and unsubstituted  
20 heterocycloxyalkyl groups, substituted and unsubstituted  
21 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
22 groups, and substituted and unsubstituted aryloxyalkyl groups;

23 Z is selected from the group consisting of O, S, and  
24 NR<sup>14</sup> groups;

25 R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> may be the same or different and  
26 are independently selected from the group consisting of H, Cl, Br, F,  
27 I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted and  
28 unsubstituted amidinyl groups, substituted and unsubstituted  
29 guanidinyl groups, substituted and unsubstituted primary, secondary,  
30 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
31 substituted and unsubstituted alkenyl groups, substituted and  
32 unsubstituted alkynyl groups, substituted and unsubstituted  
33 heterocycl groups, substituted and unsubstituted aminoalkyl groups,  
34 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
35 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
36 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
37 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,

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38 substituted and unsubstituted heterocyclalkyl groups, and -  
39 C(=O)R<sup>18</sup> groups;

40 R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> may be the same or different and  
41 are independently selected from the group consisting of H, Cl, Br, F,  
42 I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups,  
43 -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted and  
44 unsubstituted amidinyl groups, substituted and unsubstituted  
45 guanidinyl groups, substituted and unsubstituted primary, secondary,  
46 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
47 substituted and unsubstituted alkenyl groups, substituted and  
48 unsubstituted alkynyl groups, substituted and unsubstituted  
49 heterocycl groups, substituted and unsubstituted alkylaminoalkyl  
50 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
51 substituted and unsubstituted arylaminoalkyl groups, substituted and  
52 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
53 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
54 heterocyclalkyl groups, -C(=O)R<sup>25</sup> groups, substituted and  
55 unsubstituted aminoalkyl groups, substituted and unsubstituted  
56 heterocyclaminoalkyl groups, substituted and unsubstituted  
57 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
58 groups, substituted and unsubstituted aryloxyalkyl groups, and  
59 substituted and unsubstituted heterocycloxyalkyl groups;

60 R<sup>9</sup> and R<sup>14</sup> may be the same or different and are  
61 independently selected from the group consisting of H, -OH,  
62 substituted and unsubstituted alkoxy groups, substituted and  
63 unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted and unsubstituted  
64 alkylamino groups, substituted and unsubstituted arylamino groups,  
65 substituted and unsubstituted dialkylamino groups, substituted and

66 unsubstituted diarylamino groups, substituted and unsubstituted  
67 (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
68 substituted and unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl  
69 groups, and -C(=O)-aryl groups;

70  $R^{10}$  is selected from the group consisting of substituted  
71 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
72 groups, substituted and unsubstituted heterocyclyl groups, substituted  
73 and unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl  
74 groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl  
75 groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)  
76 groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
77 -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
78 groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups,  
79 -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups,  
80 -C(=O)N(alkyl)(heterocyclyl) groups, and  
81 -C(=O)N(aryl)(heterocyclyl) groups;

82  $R^{11}$  is selected from the group consisting of H, -OH,  
83 alkoxy groups, aryloxy groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
84 groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups,  
85 substituted and unsubstituted alkyl groups, -NH(heterocyclyl) groups,  
86 -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, and  
87 substituted and unsubstituted aryl groups;

88  $R^{12}$  is selected from the group consisting of H,  
89 substituted and unsubstituted alkyl groups, substituted and  
90 unsubstituted aryl groups, and substituted and unsubstituted  
91 heterocyclyl groups;

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92  $R^{13}$  is selected from the group consisting of H,  
93 substituted and unsubstituted alkyl groups, substituted and  
94 unsubstituted aryl groups, substituted and unsubstituted heterocycl  
95 groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted and  
96 unsubstituted heterocyclalkyl groups, substituted and unsubstituted  
97 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
98 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
99 substituted and unsubstituted arylaminoalkyl groups, substituted and  
100 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
101 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
102 alkylamino groups, substituted and unsubstituted arylamino groups,  
103 substituted and unsubstituted dialkylamino groups, substituted and  
104 unsubstituted diarylamino groups, substituted and unsubstituted  
105 (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-  
106 aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -  
107 C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,  
108 -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
109 -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocycl groups,  
110 -C(=O)-O-heterocycl groups, -C(=O)NH(heterocycl) groups,  
111 -C(=O)-N(heterocycl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocycl)  
112 groups, -C(=O)-N(aryl)(heterocycl) groups, substituted and  
113 unsubstituted heterocyclaminoalkyl groups, substituted and  
114 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
115 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
116 groups, and substituted and unsubstituted heterocycloxyalkyl  
117 groups;

118  $R^{15}$  and  $R^{19}$  may be the same or different and are  
119 independently selected from the group consisting of substituted and  
120 unsubstituted alkyl groups, substituted and unsubstituted aryl groups,



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121 substituted and unsubstituted heterocyclyl groups, substituted and  
122 unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl  
123 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)  
124 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -  
125 C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted  
126 and unsubstituted aminoalkyl groups, substituted and unsubstituted  
127 alkylaminoalkyl groups, substituted and unsubstituted  
128 dialkylaminoalkyl groups, substituted and unsubstituted  
129 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
130 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
131 substituted and unsubstituted heterocyclylaminoalkyl, substituted and  
132 unsubstituted diheterocyclylaminoalkyl, substituted and unsubstituted  
133 (heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted  
134 (heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted  
135 alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl  
136 groups, substituted and unsubstituted aryloxyalkyl groups, and  
137 substituted and unsubstituted heterocycloxyalkyl groups;

138 R<sup>16</sup> and R<sup>20</sup> may be the same or different and are  
139 independently selected from the group consisting of H, substituted  
140 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
141 groups, and substituted and unsubstituted heterocyclyl groups;

142 R<sup>17</sup> and R<sup>21</sup> may be the same or different and are  
143 independently selected from the group consisting of H, substituted  
144 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
145 groups, substituted and unsubstituted heterocyclyl groups, -C(=O)H,  
146 -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -  
147 C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub>  
148 groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups,

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149 -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted and  
150 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted  
151 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
152 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
153 substituted and unsubstituted arylaminoalkyl groups, substituted and  
154 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
155 (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,  
156 -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
157 -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocyclyl)  
158 groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and  
159 unsubstituted heterocyclylaminoalkyl groups, substituted and  
160 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
161 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
162 groups, and substituted and unsubstituted heterocyclyloxyalkyl  
163 groups;

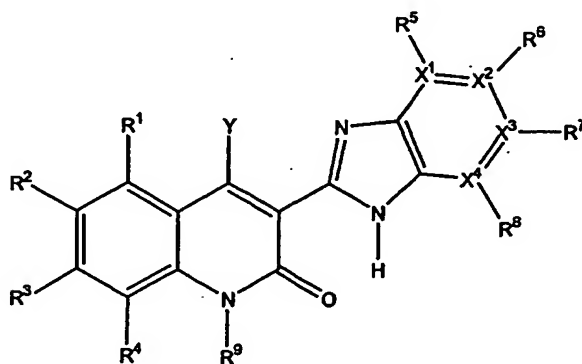
164 R<sup>18</sup>, R<sup>23</sup>, R<sup>24</sup>, and R<sup>25</sup> may be the same or different and  
165 are independently selected from the group consisting of H, -NH<sub>2</sub>,  
166 -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub>  
167 groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups,  
168 -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,  
169 -N(heterocyclyl)<sub>2</sub> groups, substituted and unsubstituted alkyl groups,  
170 substituted and unsubstituted aryl groups, -OH, substituted and  
171 unsubstituted alkoxy groups, substituted and unsubstituted aryloxy  
172 groups, substituted and unsubstituted heterocyclyl groups, -NHOH,  
173 -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups,  
174 -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, and -N(aryl)O-aryl  
175 groups; and

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176  $R^{22}$  is selected from the group consisting of substituted  
 177 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
 178 groups, and substituted and unsubstituted heterocyclyl groups,

179 and further wherein, at least one of  $R^1$ ,  $R^2$ ,  $R^3$ , or  $R^4$  is  
 180 an  $-OR^{15}$  group and  $R^{15}$  is selected from the group consisting of  
 181 substituted and unsubstituted heterocyclylalkyl groups, substituted and  
 182 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
 183 alkylaminoalkyl groups, substituted and unsubstituted aminoalkyl  
 184 groups, substituted and unsubstituted diarylaminoalkyl groups,  
 185 substituted and unsubstituted arylaminoalkyl groups, substituted and  
 186 unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and  
 187 unsubstituted heterocyclyl groups, substituted and unsubstituted  
 188 heterocyclylaminoalkyl groups, substituted and unsubstituted  
 189 diheterocyclylaminoalkyl groups, substituted and unsubstituted  
 190 (heterocyclyl)(alkyl)aminoalkyl groups, and substituted and  
 191 unsubstituted (heterocyclyl)(aryl)aminoalkyl groups.

- 1 11. A medicament, comprising: an anti-cancer drug selected from  
 2 5-FU or CPT 11 and a compound of formula II, a tautomer of the compound, a  
 3 pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable  
 4 salt of the tautomer



II

**6**                                 **wherein.**

Y is selected from the group consisting of H, -OH, -OR<sup>10</sup> groups, -SH, -SR<sup>11</sup> groups, -NR<sup>12</sup>R<sup>13</sup> groups, -CN, -C(=O)-R<sup>14</sup> groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkenyl groups, substituted and unsubstituted alkynyl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl groups, and substituted and unsubstituted heterocyclyloxyalkyl groups;

23  $X^1$ ,  $X^2$ ,  $X^3$ , and  $X^4$  are selected from the group  
24 consisting of C and N, wherein at least one of  $X^1$ ,  $X^2$ ,  $X^3$ , or  $X^4$  is N;

25  $R^1, R^2, R^3, R^4, R^5, R^6, R^7$ , and  $R^8$  may be the same or  
26 different and are independently selected from the group consisting of  
27 H, Cl, Br, F, I,  $-NO_2$ ,  $-CN$ ,  $-OH$ ,  $-OR^{15}$  groups,  $-NR^{16}R^{17}$  groups,  $-$   
28  $C(=O)R^{18}$  groups,  $-SH$ ,  $-SR^{19}$  groups,  $-S(=O)R^{20}$  groups,  $S(=O)_2R^{21}$   
29 groups, substituted and unsubstituted amidinyl groups, substituted and  
30 unsubstituted guanidinyl groups, substituted and unsubstituted  
31 primary, secondary, and tertiary alkyl groups, substituted and  
32 unsubstituted aryl groups, substituted and unsubstituted alkenyl

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33 groups, substituted and unsubstituted alkynyl groups, substituted and  
34 unsubstituted heterocyclyl groups, substituted and unsubstituted  
35 alkylaminoalkyl groups, substituted and unsubstituted  
36 dialkylaminoalkyl groups, substituted and unsubstituted  
37 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
38 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
39 substituted and unsubstituted heterocyclylalkyl groups, substituted and  
40 unsubstituted aminoalkyl groups, substituted and unsubstituted  
41 heterocyclylaminoalkyl groups, substituted and unsubstituted  
42 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
43 groups, substituted and unsubstituted aryloxyalkyl groups, and  
44 substituted and unsubstituted heterocycloxyalkyl groups; R<sup>5</sup> is  
45 absent or is H if X<sup>1</sup> is N; R<sup>6</sup> is absent or is H if X<sup>2</sup> is N; R<sup>7</sup> is absent  
46 or is H if X<sup>3</sup> is N; and R<sup>8</sup> is absent or is H if X<sup>4</sup> is N;

47 R<sup>9</sup> is selected from the group consisting of H, -OH,  
48 substituted and unsubstituted alkoxy groups, substituted and  
49 unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted and unsubstituted  
50 alkylamino groups, substituted and unsubstituted arylamino groups,  
51 substituted and unsubstituted dialkylamino groups, substituted and  
52 unsubstituted diarylamino groups, substituted and unsubstituted  
53 (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
54 substituted and unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl  
55 groups, and -C(=O)-aryl groups;

56 R<sup>10</sup> is selected from the group consisting of substituted  
57 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
58 groups, substituted and unsubstituted heterocyclyl groups, substituted  
59 and unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl  
60 groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl

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61 groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)  
62 groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
63 -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
64 groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups,  
65 -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups,  
66 -C(=O)N(alkyl)(heterocyclyl) groups, and  
67 -C(=O)N(aryl)(heterocyclyl) groups;

68 R<sup>11</sup> and R<sup>19</sup> may be the same or different and are  
69 independently selected from the group consisting of substituted and  
70 unsubstituted alkyl groups, and substituted and unsubstituted aryl  
71 groups;

72 R<sup>12</sup> is selected from the group consisting of H,  
73 substituted and unsubstituted alkyl groups, substituted and  
74 unsubstituted aryl groups, and substituted and unsubstituted  
75 heterocyclyl groups;

76 R<sup>13</sup> is selected from the group consisting of H,  
77 substituted and unsubstituted alkyl groups, substituted and  
78 unsubstituted aryl groups, substituted and unsubstituted heterocyclyl  
79 groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted and  
80 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted  
81 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
82 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
83 substituted and unsubstituted arylaminoalkyl groups, substituted and  
84 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
85 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
86 alkylamino groups, substituted and unsubstituted arylamino groups,  
87 substituted and unsubstituted dialkylamino groups, substituted and

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88 unsubstituted diarylamino groups, substituted and unsubstituted  
89 (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-  
90 aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -  
91 C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,  
92 -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
93 -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups,  
94 -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
95 -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocyclyl)  
96 groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and  
97 unsubstituted heterocyclylaminoalkyl groups, substituted and  
98 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
99 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
100 groups, and substituted and unsubstituted heterocycliloxyalkyl  
101 groups;

102 R<sup>14</sup> is selected from the group consisting of H, -OH,  
103 alkoxy groups, aryloxy groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
104 groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups,  
105 substituted and unsubstituted alkyl groups, substituted and  
106 unsubstituted aryl groups, -NH(heterocyclyl) groups,  
107 -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, and  
108 -N(aryl)(heterocyclyl) groups;

109 R<sup>12</sup> and R<sup>13</sup> may join together to form a 5 to 7  
110 membered saturated or unsaturated, substituted or unsubstituted N-  
111 containing ring;

112 R<sup>15</sup> is selected from the group consisting of substituted  
113 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
114 groups, substituted and unsubstituted heterocyclyl groups, substituted

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115 and unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl  
116 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)  
117 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups,  
118 -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted  
119 and unsubstituted aminoalkyl groups, substituted and unsubstituted  
120 alkylaminoalkyl groups, substituted and unsubstituted  
121 dialkylaminoalkyl groups, substituted and unsubstituted  
122 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
123 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
124 substituted and unsubstituted heterocyclylaminoalkyl groups,  
125 substituted and unsubstituted diheterocyclylaminoalkyl groups,  
126 substituted and unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups,  
127 substituted and unsubstituted (heterocyclyl)(aryl)aminoalkyl groups,  
128 substituted and unsubstituted alkoxyalkyl groups, substituted and  
129 unsubstituted aryloxyalkyl groups, substituted and unsubstituted  
130 hydroxyalkyl groups, and substituted and unsubstituted  
131 heterocyclyloxyalkyl groups;

132 R<sup>16</sup> is selected from the group consisting of H,  
133 substituted and unsubstituted alkyl groups, substituted and  
134 unsubstituted aryl groups, and substituted and unsubstituted  
135 heterocyclyl groups;

136 R<sup>17</sup> is selected from the group consisting of H,  
137 substituted and unsubstituted alkyl groups, substituted and  
138 unsubstituted aryl groups, substituted and unsubstituted heterocyclyl  
139 groups, OH, substituted and unsubstituted alkoxy groups, substituted  
140 and unsubstituted aryloxy groups, -NH<sub>2</sub>, -C(=O)H, -C(=O)-alkyl  
141 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)  
142 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -



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143 C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-  
144 alkyl groups, -C(=O)O-aryl groups, substituted and unsubstituted  
145 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
146 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
147 substituted and unsubstituted arylaminoalkyl groups, substituted and  
148 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
149 (aryl)(alkyl)aminoalkyl groups, substituted and unsubstituted  
150 heterocyclalkyl groups, -C(=O)-heterocycl groups,  
151 -C(=O)-Oheterocycl groups, -C(=O)NH(heterocycl) groups,  
152 -C(=O)-N(heterocycl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocycl)  
153 groups, -C(=O)-N(aryl)(heterocycl) groups, substituted and  
154 unsubstituted heterocyclaminoalkyl groups, substituted and  
155 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
156 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
157 groups, and substituted and unsubstituted heterocycloxyalkyl  
158 groups;

159 R<sup>16</sup> and R<sup>17</sup> may join together to form a 5 to 7  
160 membered saturated or unsaturated, substituted or unsubstituted N-  
161 containing ring; and

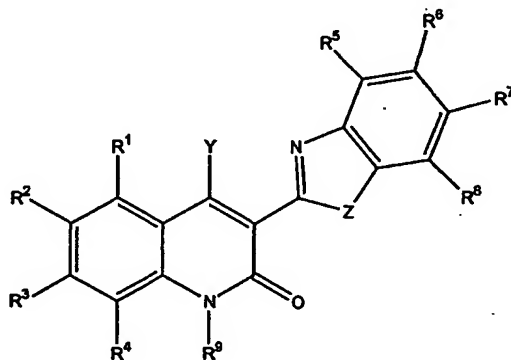
162 R<sup>18</sup>, R<sup>20</sup>, and R<sup>21</sup> may be the same or different and are  
163 independently selected from the group consisting of H, -NH<sub>2</sub>, -  
164 NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub>  
165 groups, -N(alkyl)(aryl) groups, substituted and unsubstituted alkyl  
166 groups, substituted and unsubstituted aryl groups, -OH, substituted  
167 and unsubstituted alkoxy groups, substituted and unsubstituted  
168 aryloxy groups, substituted and unsubstituted heterocycl groups, -  
169 NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl

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170 groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, and -  
 171 N(aryl)O-aryl groups.

1 12. The use of a medicament according to any of claims 1-11 in  
 2 treating cancer.

1 13. The use of a compound of formula I, a tautomer of the  
 2 compound, a pharmaceutically acceptable salt of the compound, or a  
 3 pharmaceutically acceptable salt of the tautomer in treating cancer in conjunction  
 4 with an anti-cancer drug selected from 5-FU or CPT-11



I

wherein,

5  
 6  
 7 Y is selected from the group consisting of -OR<sup>10</sup>  
 8 groups, -C(=O)-R<sup>11</sup> groups, -NR<sup>12</sup>R<sup>13</sup> groups, substituted and  
 9 unsubstituted alkynyl groups, substituted and unsubstituted  
 10 heterocyclalkyl groups, substituted and unsubstituted  
 11 alkylaminoalkyl groups, substituted and unsubstituted  
 12 dialkylaminoalkyl groups, substituted and unsubstituted  
 13 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
 14 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
 15 substituted and unsubstituted heterocyclaminoalkyl groups,  
 16 substituted and unsubstituted saturated heterocycl groups,

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17 substituted and unsubstituted heterocycloxyalkyl groups, substituted  
18 and unsubstituted hydroxyalkyl groups, and substituted and  
19 unsubstituted aryloxyalkyl groups;

20 Z is selected from the group consisting of O, S, and  
21 NR<sup>14</sup> groups;

22 R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> may be the same or different and  
23 are independently selected from the group consisting of H, Cl, Br, F,  
24 I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted and  
25 unsubstituted amidinyl groups, substituted and unsubstituted  
26 guanidinyl groups, substituted and unsubstituted primary, secondary,  
27 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
28 substituted and unsubstituted alkenyl groups, substituted and  
29 unsubstituted alkynyl groups, substituted and unsubstituted  
30 heterocyclyl groups, substituted and unsubstituted aminoalkyl groups,  
31 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
32 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
33 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
34 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
35 substituted and unsubstituted heterocyclylalkyl groups, substituted and  
36 unsubstituted diheterocyclylaminoalkyl groups, substituted and  
37 unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups, substituted and  
38 unsubstituted (heterocyclyl)(aryl)aminoalkyl groups, and -C(=O)R<sup>18</sup>  
39 groups;

40 R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> may be the same or different and  
41 are independently selected from the group consisting of H, Cl, Br, F,  
42 I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups,  
43 -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted and

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44 unsubstituted amidinyl groups, substituted and unsubstituted  
45 guanidinyl groups, substituted and unsubstituted primary, secondary,  
46 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
47 substituted and unsubstituted alkenyl groups, substituted and  
48 unsubstituted alkynyl groups, substituted and unsubstituted  
49 heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl  
50 groups,  $-C(=O)R^{25}$  groups, substituted and unsubstituted aminoalkyl  
51 groups, substituted and unsubstituted alkylaminoalkyl groups,  
52 substituted and unsubstituted dialkylaminoalkyl groups, substituted  
53 and unsubstituted arylaminoalkyl groups, substituted and  
54 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
55 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
56 heterocyclylaminoalkyl groups, substituted and unsubstituted  
57 diheterocyclylaminoalkyl groups, substituted and unsubstituted  
58 (heterocyclyl)(alkyl)aminoalkyl groups, substituted and unsubstituted  
59 (heterocyclyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
60 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
61 groups, substituted and unsubstituted aryloxyalkyl groups, and  
62 substituted and unsubstituted heterocyclyoxyalkyl groups;

63  $R^9$  and  $R^{14}$  may be the same or different and are  
64 independently selected from the group consisting of H, -OH,  
65 substituted and unsubstituted alkoxy groups, substituted and  
66 unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted and unsubstituted  
67 alkylamino groups, substituted and unsubstituted arylamino groups,  
68 substituted and unsubstituted dialkylamino groups, substituted and  
69 unsubstituted diarylamino groups, substituted and unsubstituted  
70 (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
71 substituted and unsubstituted aryl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl  
72 groups, and  $-C(=O)$ -aryl groups;

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73  $R^{10}$  is selected from the group consisting of substituted  
74 and unsubstituted aryl groups, substituted and unsubstituted  
75 heterocyclyl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl groups,  $-C(=O)$ -aryl  
76 groups,  $-C(=O)O$ -alkyl groups,  $-C(=O)O$ -aryl groups,  $-C(=O)NH_2$ ,  
77  $-C(=O)NH$ (alkyl) groups,  $-C(=O)NH$ (aryl) groups,  
78  $-C(=O)N$ (alkyl)<sub>2</sub> groups,  $-C(=O)N$ (aryl)<sub>2</sub> groups,  
79  $-C(=O)N$ (alkyl)(aryl) groups,  $-NH_2$ ,  $-NH$ (alkyl) groups,  $-NH$ (aryl)  
80 groups,  $-N$ (alkyl)<sub>2</sub> groups,  $-N$ (alkyl)(aryl) groups,  $-N$ (aryl)<sub>2</sub> groups,  
81  $-NH$ (heterocyclyl) groups,  $-N$ (heterocyclyl)<sub>2</sub> groups,  
82  $-N$ (alkyl)(heterocyclyl) groups,  $-N$ (aryl)(heterocyclyl),  
83  $-C(=O)NH$ (heterocyclyl) groups,  $-C(=O)N$ (heterocyclyl)<sub>2</sub> groups,  
84  $-C(=O)N$ (alkyl)(heterocyclyl) groups,  $-C(=O)N$ (aryl)(heterocyclyl)  
85 groups, and substituted and unsubstituted heterocyclylalkyl groups;

86  $R^{11}$  is selected from the group consisting of  $H$ ,  $-NH_2$ , -  
87  $NH$ (alkyl) groups,  $-NH$ (aryl) groups,  $-N$ (alkyl)<sub>2</sub> groups,  $-N$ (aryl)<sub>2</sub>  
88 groups,  $-N$ (alkyl)(aryl) groups,  $-NH$ (heterocyclyl) groups, -  
89  $N$ (heterocyclyl)<sub>2</sub> groups,  $-N$ (alkyl)(heterocyclyl) groups, -  
90  $N$ (aryl)(heterocyclyl) groups,  $-O$ -alkyl groups,  $O$ -aryl groups,  
91 heterocycloxyalkyl groups, and substituted and unsubstituted aryl  
92 groups;

93  $R^{12}$  is selected from the group consisting of  $H$ ,  
94 substituted and unsubstituted alkyl groups, substituted and  
95 unsubstituted aryl groups, and substituted and unsubstituted  
96 heterocyclyl groups;

97  $R^{13}$  is selected from the group consisting of substituted  
98 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
99 groups, substituted and unsubstituted heterocyclyl groups,  $-OH$ ,

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100 alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted and unsubstituted  
101 heterocyclalkyl groups, substituted and unsubstituted aminoalkyl  
102 groups, substituted and unsubstituted alkylaminoalkyl groups,  
103 substituted and unsubstituted dialkylaminoalkyl groups, substituted  
104 and unsubstituted arylaminoalkyl groups, substituted and  
105 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
106 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
107 alkylamino groups, substituted and unsubstituted arylamino groups,  
108 substituted and unsubstituted dialkylamino groups, substituted and  
109 unsubstituted diarylamino groups, substituted and unsubstituted  
110 (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-  
111 aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -  
112 C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,  
113 -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
114 -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclalkyl groups,  
115 -C(=O)-O-heterocyclalkyl groups, -C(=O)NH(heterocyclalkyl) groups,  
116 -C(=O)-N(heterocyclalkyl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocyclalkyl)  
117 groups, substituted and unsubstituted heterocyclalkylaminoalkyl groups,  
118 substituted and unsubstituted hydroxyalkyl groups, substituted and  
119 unsubstituted alkoxyalkyl groups, substituted and unsubstituted  
120 aryloxyalkyl groups, substituted and unsubstituted  
121 heterocyclalkyloxyalkyl groups, and -C(=O)-N(alkyl)(heterocyclalkyl)  
122 groups;

123 R<sup>15</sup> and R<sup>19</sup> may be the same or different and are  
124 independently selected from the group consisting of substituted and  
125 unsubstituted alkyl groups, substituted and unsubstituted aryl groups,  
126 substituted and unsubstituted heterocyclalkyl groups, substituted and  
127 unsubstituted heterocyclalkyl groups, -C(=O)H, -C(=O)-alkyl  
128 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)

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129 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -  
 130 C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -  
 131 NH(heterocyclyl) groups, -N(heterocyclyl)<sub>2</sub> groups, -  
 132 N(alkyl)(heterocyclyl) groups, -N(aryl)(heterocyclyl) groups,  
 133 substituted and unsubstituted aminoalkyl groups, substituted and  
 134 unsubstituted alkylaminoalkyl groups, substituted and unsubstituted  
 135 dialkylaminoalkyl groups, substituted and unsubstituted  
 136 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
 137 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
 138 substituted and unsubstituted heterocyclylaminoalkyl, substituted and  
 139 unsubstituted diheterocyclylaminoalkyl, substituted and unsubstituted  
 140 (heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted  
 141 (heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted  
 142 alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl  
 143 groups, substituted and unsubstituted aryloxyalkyl groups, and  
 144 substituted and unsubstituted heterocycliloxyalkyl groups;

145 R<sup>16</sup> and R<sup>20</sup> may be the same or different and are  
 146 independently selected from the group consisting of H, substituted  
 147 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
 148 groups, and substituted and unsubstituted heterocyclyl groups;

149 R<sup>17</sup> and R<sup>21</sup> may be the same or different and are  
 150 independently selected from the group consisting of H, substituted  
 151 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
 152 groups, substituted and unsubstituted heterocyclyl groups, -C(=O)H,  
 153 -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -  
 154 C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub>  
 155 groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups,  
 156 -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted and

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157 unsubstituted heterocyclalkyl groups, substituted and unsubstituted  
158 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
159 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
160 substituted and unsubstituted arylaminoalkyl groups, substituted and  
161 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
162 (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocycl groups,  
163 -C(=O)-O-heterocycl groups, -C(=O)NH(heterocycl) groups,  
164 -C(=O)N(heterocycl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocycl)  
165 groups, substituted and unsubstituted heterocyclaminoalkyl groups,  
166 substituted and unsubstituted diheterocyclaminoalkyl groups,  
167 substituted and unsubstituted (heterocycl)(alkyl)aminoalkyl groups,  
168 substituted and unsubstituted (heterocycl)(aryl)aminoalkyl groups,  
169 substituted and unsubstituted hydroxyalkyl groups, substituted and  
170 unsubstituted alkoxyalkyl groups, substituted and unsubstituted  
171 aryloxyalkyl groups, substituted and unsubstituted  
172 heterocycloxyalkyl groups, and -C(=O)-N(alkyl)(heterocycl)  
173 groups;

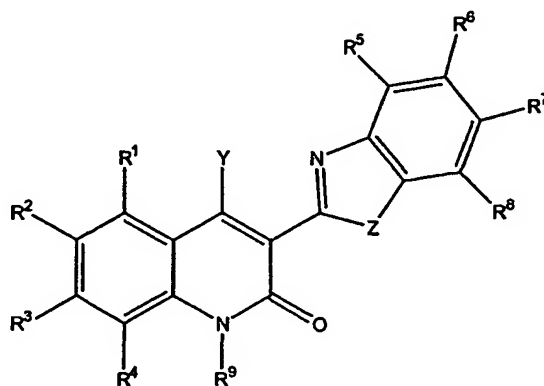
174  $R^{18}$ ,  $R^{23}$ ,  $R^{24}$ , and  $R^{25}$  may be the same or different and  
175 are independently selected from the group consisting of H, -NH<sub>2</sub>,  
176 -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub>  
177 groups, -N(alkyl)(aryl) groups, -NH(heterocycl) groups,  
178 -N(heterocycl)(alkyl) groups, -N(heterocycl)(aryl) groups,  
179 -N(heterocycl)<sub>2</sub> groups, substituted and unsubstituted alkyl groups,  
180 substituted and unsubstituted aryl groups, -OH, substituted and  
181 unsubstituted alkoxy groups, substituted and unsubstituted  
182 heterocycl groups, substituted and unsubstituted aryloxy groups,  
183 heterocycloxy groups, -NHOH, -N(alkyl)OH groups, -N(aryl)OH  
184 groups, -N(alkyl)O-alkyl groups, -N(aryl)O-alkyl groups, -N(alkyl)O-  
185 aryl groups, and -N(aryl)O-aryl groups; and



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186  $R^{22}$  is selected from the group consisting of substituted  
 187 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
 188 groups, and substituted and unsubstituted heterocyclyl groups.

1 14. The use of a compound of formula I, a tautomer of the  
 2 compound, a pharmaceutically acceptable salt of the compound, or a  
 3 pharmaceutically acceptable salt of the tautomer in treating cancer in conjunction  
 4 with an anti-cancer drug selected from 5-FU or CPT-11



5  
6

I  
 wherein,

7 Y is selected from the group consisting of  $-OR^{10}$   
 8 groups,  $-C(=O)-R^{11}$  groups,  $-NR^{12}R^{13}$  groups, substituted and  
 9 unsubstituted alkynyl groups, substituted and unsubstituted  
 10 heterocyclalkyl groups, substituted and unsubstituted  
 11 alkylaminoalkyl groups, substituted and unsubstituted  
 12 dialkylaminoalkyl groups, substituted and unsubstituted  
 13 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
 14 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
 15 substituted and unsubstituted heterocyclaminoalkyl groups,  
 16 substituted and unsubstituted saturated heterocyclyl groups,  
 17 substituted and unsubstituted heterocycloxyalkyl groups, substituted

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18 and unsubstituted hydroxyalkyl groups, and substituted and  
19 unsubstituted aryloxyalkyl groups;

20 Z is selected from the group consisting of O, S, and  
21 NR<sup>14</sup> groups;

22 R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> may be the same or different and  
23 are independently selected from the group consisting of H, Cl, Br, F,  
24 I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted and  
25 unsubstituted amidinyl groups, substituted and unsubstituted  
26 guanidinyl groups, substituted and unsubstituted primary, secondary,  
27 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
28 substituted and unsubstituted alkenyl groups, substituted and  
29 unsubstituted alkynyl groups, substituted and unsubstituted  
30 heterocyclyl groups, substituted and unsubstituted aminoalkyl groups,  
31 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
32 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
33 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
34 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
35 substituted and unsubstituted heterocyclylalkyl groups, and -  
36 C(=O)R<sup>18</sup> groups;

37 R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> may be the same or different and  
38 are independently selected from the group consisting of H, Cl, Br, F,  
39 I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups,  
40 -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted and  
41 unsubstituted amidinyl groups, substituted and unsubstituted  
42 guanidinyl groups, substituted and unsubstituted primary, secondary,  
43 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
44 substituted and unsubstituted alkenyl groups, substituted and

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45 unsubstituted alkynyl groups, substituted and unsubstituted  
46 heterocyclyl groups, substituted and unsubstituted heterocyclylalkyl  
47 groups,  $-C(=O)R^{25}$  groups, substituted and unsubstituted aminoalkyl  
48 groups, substituted and unsubstituted alkylaminoalkyl groups,  
49 substituted and unsubstituted dialkylaminoalkyl groups, substituted  
50 and unsubstituted arylaminoalkyl groups, substituted and  
51 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
52 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
53 heterocyclylaminoalkyl groups, substituted and unsubstituted  
54 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
55 groups, substituted and unsubstituted aryloxyalkyl groups, and  
56 substituted and unsubstituted heterocycloxyalkyl groups;

57  $R^9$  is selected from the group consisting of -OH,  
58 substituted and unsubstituted alkoxy groups, substituted and  
59 unsubstituted aryloxy groups,  $-NH_2$ , substituted and unsubstituted  
60 alkylamino groups, substituted and unsubstituted arylamino groups,  
61 substituted and unsubstituted dialkylamino groups, substituted and  
62 unsubstituted diarylamino groups, substituted and unsubstituted  
63 (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
64 substituted and unsubstituted aryl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl  
65 groups, and  $-C(=O)$ -aryl groups;

66  $R^{10}$  is selected from the group consisting of substituted  
67 and unsubstituted aryl groups, substituted and unsubstituted  
68 heterocyclyl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl groups,  $-C(=O)$ -aryl  
69 groups,  $-C(=O)O$ -alkyl groups,  $-C(=O)O$ -aryl groups,  $-C(=O)NH_2$ ,  
70  $-C(=O)NH$ (alkyl) groups,  $-C(=O)NH$ (aryl) groups,  
71  $-C(=O)N$ (alkyl)<sub>2</sub> groups,  $-C(=O)N$ (aryl)<sub>2</sub> groups,  
72  $-C(=O)N$ (alkyl)(aryl) groups,  $-NH_2$ ,  $-NH$ (alkyl) groups,  $-NH$ (aryl)

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73 groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups,  
74 -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups,  
75 -C(=O)N(alkyl)(heterocyclyl) groups, -C(=O)N(aryl)(heterocyclyl)  
76 groups, and substituted and unsubstituted heterocyclylalkyl groups;

77 R<sup>11</sup> is selected from the group consisting of H, -NH<sub>2</sub>, -  
78 NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub>  
79 groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups, -  
80 N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, -O-alkyl  
81 groups, O-aryl groups, substituted and unsubstituted alkyl groups,  
82 and substituted and unsubstituted aryl groups;

83 R<sup>12</sup> is selected from the group consisting of H,  
84 substituted and unsubstituted alkyl groups, substituted and  
85 unsubstituted aryl groups, and substituted and unsubstituted  
86 heterocyclyl groups;

87 R<sup>13</sup> is selected from the group consisting of H,  
88 substituted and unsubstituted alkyl groups, substituted and  
89 unsubstituted aryl groups, substituted and unsubstituted heterocyclyl  
90 groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted and  
91 unsubstituted alkylamino groups, substituted and unsubstituted  
92 arylamino groups, substituted and unsubstituted dialkylamino groups,  
93 substituted and unsubstituted diarylamino groups, substituted and  
94 unsubstituted (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl  
95 groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl  
96 groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)  
97 groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
98 -C(=O)N(alkyl)(aryl) groups, substituted and unsubstituted  
99 heterocyclylalkyl groups, substituted and unsubstituted aminoalkyl

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100 groups, substituted and unsubstituted alkylaminoalkyl groups,  
101 substituted and unsubstituted dialkylaminoalkyl groups, substituted  
102 and unsubstituted arylaminoalkyl groups, substituted and  
103 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
104 (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,  
105 -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
106 -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocyclyl)  
107 groups, -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and  
108 unsubstituted heterocyclylaminoalkyl groups, substituted and  
109 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
110 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
111 groups, and substituted and unsubstituted heterocyclioxyalkyl  
112 groups;

113 R<sup>14</sup> is selected from the group consisting of H, -OH,  
114 substituted and unsubstituted alkoxy groups, substituted and  
115 unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted and unsubstituted  
116 alkylamino groups, substituted and unsubstituted arylamino groups,  
117 substituted and unsubstituted dialkylamino groups, substituted and  
118 unsubstituted diarylamino groups, substituted and unsubstituted  
119 (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
120 substituted and unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl  
121 groups, and -C(=O)-aryl groups;

122 R<sup>15</sup> and R<sup>19</sup> may be the same or different and are  
123 independently selected from the group consisting of substituted and  
124 unsubstituted alkyl groups, substituted and unsubstituted aryl groups,  
125 substituted and unsubstituted heterocyclyl groups, substituted and  
126 unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl  
127 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)

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128 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -  
129 C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted  
130 and unsubstituted aminoalkyl groups, substituted and unsubstituted  
131 alkylaminoalkyl groups, substituted and unsubstituted  
132 dialkylaminoalkyl groups, substituted and unsubstituted  
133 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
134 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
135 substituted and unsubstituted heterocyclylaminoalkyl, substituted and  
136 unsubstituted diheterocyclylaminoalkyl, substituted and unsubstituted  
137 (heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted  
138 (heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted  
139 alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl  
140 groups, substituted and unsubstituted aryloxyalkyl groups, and  
141 substituted and unsubstituted heterocyclyloxyalkyl groups;

142 R<sup>16</sup> and R<sup>20</sup> may be the same or different and are  
143 independently selected from the group consisting of H, substituted  
144 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
145 groups, and substituted and unsubstituted heterocyclyl groups;

146 R<sup>17</sup> and R<sup>21</sup> may be the same or different and are  
147 independently selected from the group consisting of H, substituted  
148 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
149 groups, substituted and unsubstituted heterocyclyl groups, -C(=O)H,  
150 -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -  
151 C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub>  
152 groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups,  
153 -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted and  
154 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted  
155 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl

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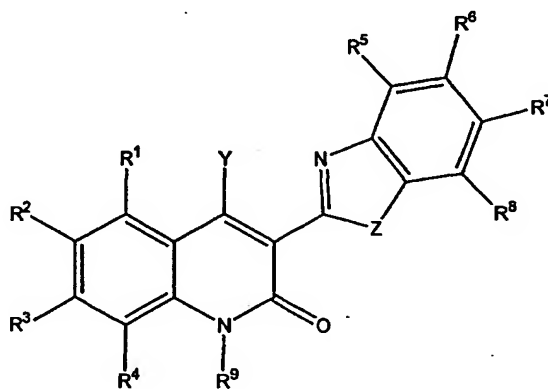
156 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
157 substituted and unsubstituted arylaminoalkyl groups, substituted and  
158 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
159 (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,  
160 -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
161 -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)N(aryl)(heterocyclyl)  
162 groups, -C(=O)-N(alkyl)(heterocyclyl) groups, substituted and  
163 unsubstituted heterocyclylaminoalkyl groups, substituted and  
164 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
165 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
166 groups, and substituted and unsubstituted heterocycloxyalkyl  
167 groups;

168  $R^{18}$ ,  $R^{23}$ ,  $R^{24}$ , and  $R^{25}$  may be the same or different and  
169 are independently selected from the group consisting of H, -NH<sub>2</sub>,  
170 -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub>  
171 groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups,  
172 -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,  
173 -N(heterocyclyl)<sub>2</sub> groups, substituted and unsubstituted alkyl groups,  
174 substituted and unsubstituted aryl groups, -OH, substituted and  
175 unsubstituted alkoxy groups, substituted and unsubstituted  
176 heterocyclyl groups, substituted and unsubstituted aryloxy groups,  
177 -NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl  
178 groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, and  
179 -N(aryl)O-aryl groups; and

180  $R^{22}$  is selected from the group consisting of substituted  
181 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
182 groups, and substituted and unsubstituted heterocyclyl groups.

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- 1                    15.    The use of a compound of formula I, a tautomer of the  
 2    compound, a pharmaceutically acceptable salt of the compound, or a  
 3    pharmaceutically acceptable salt of the tautomer in treating cancer in conjunction  
 4    with an anti-cancer drug selected from 5-FU or CPT-11



I

wherein,

- 7                    Y is selected from the group consisting of -OH, SH,  
 8    alkylthio groups, arylthio groups, -OR<sup>10</sup> groups, -C(=O)-R<sup>11</sup> groups,  
 9    -NR<sup>12</sup>R<sup>13</sup> groups, -CN, substituted and unsubstituted alkyl groups,  
 10    substituted and unsubstituted alkenyl groups, substituted and  
 11    unsubstituted alkynyl groups, substituted and unsubstituted aralkyl  
 12    groups, substituted and unsubstituted heterocyclylalkyl groups,  
 13    substituted and unsubstituted alkylaminoalkyl groups, substituted and  
 14    unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
 15    arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
 16    groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
 17    substituted and unsubstituted heterocyclylaminoalkyl groups,  
 18    substituted and unsubstituted heterocyclyl groups, substituted and  
 19    unsubstituted aryl groups, substituted and unsubstituted  
 20    heterocyclyloxyalkyl groups, substituted and unsubstituted



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21 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
22 groups, and substituted and unsubstituted aryloxyalkyl groups;

23 Z is selected from the group consisting of O, S, and  
24 NR<sup>14</sup> groups;

25 R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> may be the same or different and  
26 are independently selected from the group consisting of H, Cl, Br, F,  
27 I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted and  
28 unsubstituted amidinyl groups, substituted and unsubstituted  
29 guanidinyl groups, substituted and unsubstituted primary, secondary,  
30 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
31 substituted and unsubstituted alkenyl groups, substituted and  
32 unsubstituted alkynyl groups, substituted and unsubstituted  
33 heterocyclyl groups, substituted and unsubstituted aminoalkyl groups,  
34 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
35 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
36 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
37 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
38 substituted and unsubstituted heterocyclylalkyl groups, and -  
39 C(=O)R<sup>18</sup> groups;

40 R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> may be the same or different and  
41 are independently selected from the group consisting of H, Cl, Br, F,  
42 I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups,  
43 -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted and  
44 unsubstituted amidinyl groups, substituted and unsubstituted  
45 guanidinyl groups, substituted and unsubstituted primary, secondary,  
46 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
47 substituted and unsubstituted alkenyl groups, substituted and

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48 unsubstituted alkynyl groups, substituted and unsubstituted  
49 heterocyclyl groups, substituted and unsubstituted alkylaminoalkyl  
50 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
51 substituted and unsubstituted arylaminoalkyl groups, substituted and  
52 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
53 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
54 heterocyclylalkyl groups,  $-C(=O)R^{25}$  groups, substituted and  
55 unsubstituted aminoalkyl groups, substituted and unsubstituted  
56 heterocyclylaminoalkyl groups, substituted and unsubstituted  
57 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
58 groups, substituted and unsubstituted aryloxyalkyl groups, and  
59 substituted and unsubstituted heterocyclyloxyalkyl groups;

60  $R^9$  and  $R^{14}$  may be the same or different and are  
61 independently selected from the group consisting of H, -OH,  
62 substituted and unsubstituted alkoxy groups, substituted and  
63 unsubstituted aryloxy groups,  $-NH_2$ , substituted and unsubstituted  
64 alkylamino groups, substituted and unsubstituted arylamino groups,  
65 substituted and unsubstituted dialkylamino groups, substituted and  
66 unsubstituted diarylamino groups, substituted and unsubstituted  
67 (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
68 substituted and unsubstituted aryl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl  
69 groups, and  $-C(=O)$ -aryl groups;

70  $R^{10}$  is selected from the group consisting of substituted  
71 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
72 groups, substituted and unsubstituted heterocyclyl groups, substituted  
73 and unsubstituted heterocyclylalkyl groups,  $-C(=O)H$ ,  $-C(=O)$ -alkyl  
74 groups,  $-C(=O)$ -aryl groups,  $-C(=O)O$ -alkyl groups,  $-C(=O)O$ -aryl  
75 groups,  $-C(=O)NH_2$ ,  $-C(=O)NH$ (alkyl) groups,  $-C(=O)NH$ (aryl)

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76 groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
77 -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
78 groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups,  
79 -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups,  
80 -C(=O)N(alkyl)(heterocyclyl) groups, and  
81 -C(=O)N(aryl)(heterocyclyl) groups;

82 R<sup>11</sup> is selected from the group consisting of H, -OH,  
83 alkoxy groups, aryloxy groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
84 groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups,  
85 substituted and unsubstituted alkyl groups, -NH(heterocyclyl) groups,  
86 -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, and  
87 substituted and unsubstituted aryl groups;

88 R<sup>12</sup> is selected from the group consisting of H,  
89 substituted and unsubstituted alkyl groups, substituted and  
90 unsubstituted aryl groups, and substituted and unsubstituted  
91 heterocyclyl groups;

92 R<sup>13</sup> is selected from the group consisting of H,  
93 substituted and unsubstituted alkyl groups, substituted and  
94 unsubstituted aryl groups, substituted and unsubstituted heterocyclyl  
95 groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted and  
96 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted  
97 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
98 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
99 substituted and unsubstituted arylaminoalkyl groups, substituted and  
100 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
101 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
102 alkylamino groups, substituted and unsubstituted arylamino groups,

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103 substituted and unsubstituted dialkylamino groups, substituted and  
104 unsubstituted diarylamino groups, substituted and unsubstituted  
105 (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-  
106 aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -  
107 C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,  
108 -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
109 -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups,  
110 -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
111 -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocyclyl)  
112 groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and  
113 unsubstituted heterocyclylaminoalkyl groups, substituted and  
114 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
115 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
116 groups, and substituted and unsubstituted heterocyclyoxyalkyl  
117 groups;

118 R<sup>15</sup> and R<sup>19</sup> may be the same or different and are  
119 independently selected from the group consisting of substituted and  
120 unsubstituted alkyl groups, substituted and unsubstituted aryl groups,  
121 substituted and unsubstituted heterocyclyl groups, substituted and  
122 unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl  
123 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)  
124 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -  
125 C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted  
126 and unsubstituted aminoalkyl groups, substituted and unsubstituted  
127 alkylaminoalkyl groups, substituted and unsubstituted  
128 dialkylaminoalkyl groups, substituted and unsubstituted  
129 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
130 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
131 substituted and unsubstituted heterocyclylaminoalkyl, substituted and

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132 unsubstituted diheterocyclylaminoalkyl, substituted and unsubstituted  
133 (heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted  
134 (heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted  
135 alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl  
136 groups, substituted and unsubstituted aryloxyalkyl groups, and  
137 substituted and unsubstituted heterocycloxyalkyl groups;

138  $R^{16}$  and  $R^{20}$  may be the same or different and are  
139 independently selected from the group consisting of H, substituted  
140 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
141 groups, and substituted and unsubstituted heterocyclyl groups;

142  $R^{17}$  and  $R^{21}$  may be the same or different and are  
143 independently selected from the group consisting of H, substituted  
144 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
145 groups, substituted and unsubstituted heterocyclyl groups,  $-C(=O)H$ ,  
146  $-C(=O)$ -alkyl groups,  $-C(=O)$ -aryl groups,  $-C(=O)NH_2$ , -  
147  $C(=O)NH$ (alkyl) groups,  $-C(=O)NH$ (aryl) groups,  $-C(=O)N$ (alkyl)<sub>2</sub>  
148 groups,  $-C(=O)N$ (aryl)<sub>2</sub> groups,  $-C(=O)N$ (alkyl)(aryl) groups,  
149  $-C(=O)O$ -alkyl groups,  $-C(=O)O$ -aryl groups, substituted and  
150 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted  
151 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
152 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
153 substituted and unsubstituted arylaminoalkyl groups, substituted and  
154 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
155 (alkyl)(aryl)aminoalkyl groups,  $-C(=O)$ -heterocyclyl groups,  
156  $-C(=O)-O$ -heterocyclyl groups,  $-C(=O)NH$ (heterocyclyl) groups,  
157  $-C(=O)-N$ (heterocyclyl)<sub>2</sub> groups,  $-C(=O)-N$ (alkyl)(heterocyclyl)  
158 groups,  $-C(=O)-N$ (aryl)(heterocyclyl) groups, substituted and  
159 unsubstituted heterocyclylaminoalkyl groups, substituted and

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160 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
161 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
162 groups, and substituted and unsubstituted heterocycloxyalkyl  
163 groups;

164  $R^{18}$ ,  $R^{23}$ ,  $R^{24}$ , and  $R^{25}$  may be the same or different and  
165 are independently selected from the group consisting of H,  $-NH_2$ ,  
166  $-NH(alkyl)$  groups,  $-NH(aryl)$  groups,  $-N(alkyl)_2$  groups,  $-N(aryl)_2$   
167 groups,  $-N(alkyl)(aryl)$  groups,  $-NH(heterocyclyl)$  groups,  
168  $-N(heterocyclyl)(alkyl)$  groups,  $-N(heterocyclyl)(aryl)$  groups,  
169  $-N(heterocyclyl)_2$  groups, substituted and unsubstituted alkyl groups,  
170 substituted and unsubstituted aryl groups,  $-OH$ , substituted and  
171 unsubstituted alkoxy groups, substituted and unsubstituted aryloxy  
172 groups, substituted and unsubstituted heterocyclyl groups,  $-NHOH$ ,  
173  $-N(alkyl)OH$  groups,  $-N(aryl)OH$  groups,  $-N(alkyl)O-alkyl$  groups,  
174  $-N(aryl)O-alkyl$  groups,  $-N(alkyl)O-aryl$  groups, and  $-N(aryl)O-aryl$   
175 groups; and

176  $R^{22}$  is selected from the group consisting of substituted  
177 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
178 groups, and substituted and unsubstituted heterocyclyl groups;

179 and further wherein at least one of  $R^5$ ,  $R^6$ ,  $R^7$ , or  $R^8$  is  
180 selected from the group consisting of substituted and unsubstituted  
181 amidinyl groups, substituted and unsubstituted guanidinyl groups,  
182 substituted and unsubstituted saturated heterocyclyl groups,  
183 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
184 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
185 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
186 groups, substituted and unsubstituted  $(alkyl)(aryl)aminoalkyl$  groups,

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187 substituted and unsubstituted heterocyclalkyl groups, substituted and  
188 unsubstituted heterocyclaminoalkyl groups, substituted and  
189 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
190 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
191 groups, and substituted and unsubstituted heterocycloxyalkyl  
192 groups;  $-OR^{19}$  groups wherein  $R^{19}$  is selected from the group  
193 consisting of substituted and unsubstituted aryl groups, substituted  
194 and unsubstituted heterocycl groups, substituted and unsubstituted  
195 heterocyclalkyl groups,  $-C(=O)H$ ,  $-C(=O)$ -aryl groups,  
196  $-C(=O)NH_2$ ,  $-C(=O)NH(alkyl)$  groups,  $-C(=O)NH(aryl)$  groups,  
197  $-C(=O)N(alkyl)_2$  groups,  $-C(=O)N(aryl)_2$  groups,  
198  $-C(=O)N(alkyl)(aryl)$  groups, substituted and unsubstituted  
199 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
200 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
201 substituted and unsubstituted arylaminoalkyl groups, substituted and  
202 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
203 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
204 heterocyclaminoalkyl groups, substituted and unsubstituted  
205 diheterocyclaminoalkyl groups, substituted and unsubstituted  
206 (heterocycl)(alkyl)aminoalkyl groups, substituted and unsubstituted  
207 (heterocycl)(aryl)aminoalkyl groups, substituted and unsubstituted  
208 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
209 groups, substituted and unsubstituted aryloxyalkyl groups, and  
210 substituted and unsubstituted heterocycloxyalkyl groups;  $-NR^{20}R^{21}$   
211 groups wherein  $R^{20}$  is selected from the group consisting of  
212 substituted and unsubstituted heterocycl groups;  $-NR^{20}R^{21}$  groups  
213 wherein  $R^{21}$  is selected from the group consisting of substituted and  
214 unsubstituted heterocycl groups,  $-C(=O)H$ ,  $-C(=O)$ -aryl groups,  
215  $-C(=O)NH_2$ ,  $-C(=O)NH(alkyl)$  groups,  $-C(=O)NH(aryl)$  groups,  
216  $-C(=O)N(alkyl)_2$  groups,  $-C(=O)N(aryl)_2$  groups,

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217 -C(=O)N(alkyl)(aryl) groups, -C(=O)O-alkyl groups, -C(=O)O-aryl  
 218 groups, substituted and unsubstituted aminoalkyl groups, substituted  
 219 and unsubstituted alkylaminoalkyl groups, substituted and  
 220 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
 221 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
 222 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
 223 substituted and unsubstituted heterocyclylaminoalkyl groups,  
 224 substituted and unsubstituted hydroxyalkyl groups, substituted and  
 225 unsubstituted alkoxyalkyl groups, substituted and unsubstituted  
 226 aryloxyalkyl groups, substituted and unsubstituted heterocyclylalkyl  
 227 groups, and substituted and unsubstituted heterocyclylloxyalkyl  
 228 groups; and -C(=O)R<sup>25</sup> groups wherein R<sup>25</sup> is selected from the  
 229 group consisting of H, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl) groups, -  
 230 N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -  
 231 NH(heterocyclyl) groups, -N(heterocyclyl)(alkyl) groups, -  
 232 N(heterocyclyl)(aryl) groups, -N(heterocyclyl)<sub>2</sub> groups, substituted  
 233 and unsubstituted aryl groups, substituted and unsubstituted aryloxy  
 234 groups, and substituted and unsubstituted heterocyclyl groups.

1 16. The use according to claim 15, wherein Y is selected from the  
 2 group consisting of -OR<sup>10</sup> groups, -NR<sup>12</sup>R<sup>13</sup> groups, and substituted and  
 3 unsubstituted alkynyl groups.

1 17. The use according to claim 15, wherein Z is an -NR<sup>14</sup> group.

1 18. The use according to claim 15, wherein R<sup>1</sup> is selected from  
 2 the group consisting of -H, substituted and unsubstituted alkoxy groups, substituted  
 3 and unsubstituted heterocyclylalkoxy groups, substituted and unsubstituted  
 4 heterocyclylloxy groups, and substituted and unsubstituted heterocyclyl groups.



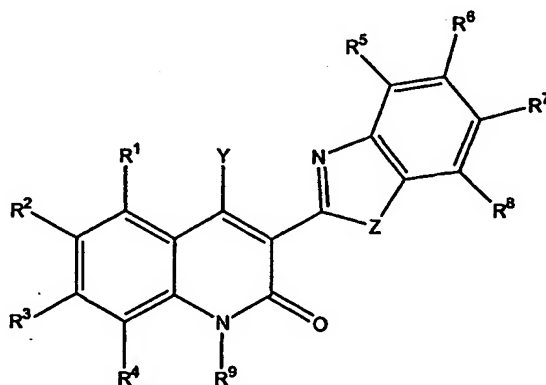
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1                    19.    The use according to claim 15, wherein  $R^2$  is selected from  
 2    the group consisting of H, F, Cl,  $-NO_2$ , substituted and unsubstituted heterocycl  
 3    groups, and substituted and unsubstituted heterocyclalkoxy groups.

1                    20.    The use according to claim 15, wherein  $R^6$  or  $R^7$  is an alkyl  
 2    group.

1                    21.    The use according to claim 15, wherein  $R^6$  or  $R^7$  is an  $-OR^{19}$   
 2    group and  $R^{19}$  is an alkyl group, an aryl group, a heterocycl group, or a  
 3    heterocyclalkyl group.

1                    22.    The use of a compound of formula I; a tautomer of the  
 2    compound, a pharmaceutically acceptable salt of the compound, or a  
 3    pharmaceutically acceptable salt of the tautomer in treating cancer in conjunction  
 4    with an anti-cancer drug selected from 5-FU or CPT-11



I

wherein,

7                    Y is selected from the group consisting of  $-OH$ ,  $SH$ ,  
 8    alkylthio groups, arylthio groups,  $-OR^{10}$  groups,  $-C(=O)-R^{11}$  groups,  
 9     $-NR^{12}R^{13}$  groups,  $-CN$ , substituted and unsubstituted alkyl groups,  
 10    substituted and unsubstituted alkenyl groups, substituted and

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11 unsubstituted alkynyl groups, substituted and unsubstituted aralkyl  
12 groups, substituted and unsubstituted heterocyclalkyl groups,  
13 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
14 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
15 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
16 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
17 substituted and unsubstituted heterocyclaminoalkyl groups,  
18 substituted and unsubstituted heterocycl groups, substituted and  
19 unsubstituted aryl groups, substituted and unsubstituted  
20 heterocycloxyalkyl groups, substituted and unsubstituted  
21 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
22 groups, and substituted and unsubstituted aryloxyalkyl groups;

23 Z is selected from the group consisting of O, S, and  
24  $\text{NR}^{14}$  groups;

25  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , and  $\text{R}^4$  may be the same or different and  
26 are independently selected from the group consisting of H, Cl, Br, F,  
27 I, -CN, -NO<sub>2</sub>, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, substituted and  
28 unsubstituted amidinyl groups, substituted and unsubstituted  
29 guanidinyl groups, substituted and unsubstituted primary, secondary,  
30 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
31 substituted and unsubstituted alkenyl groups, substituted and  
32 unsubstituted alkynyl groups, substituted and unsubstituted  
33 heterocycl groups, substituted and unsubstituted aminoalkyl groups,  
34 substituted and unsubstituted alkylaminoalkyl groups, substituted and  
35 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
36 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
37 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,

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38 substituted and unsubstituted heterocyclalkyl groups, and -  
39 C(=O)R<sup>18</sup> groups;

40 R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> may be the same or different and  
41 are independently selected from the group consisting of H, Cl, Br, F,  
42 I, -NO<sub>2</sub>, -OH, -OR<sup>19</sup> groups, -NR<sup>20</sup>R<sup>21</sup> groups, -SH, -SR<sup>22</sup> groups,  
43 -S(=O)R<sup>23</sup> groups, -S(=O)<sub>2</sub>R<sup>24</sup> groups, -CN, substituted and  
44 unsubstituted amidinyl groups, substituted and unsubstituted  
45 guanidinyl groups, substituted and unsubstituted primary, secondary,  
46 and tertiary alkyl groups, substituted and unsubstituted aryl groups,  
47 substituted and unsubstituted alkenyl groups, substituted and  
48 unsubstituted alkynyl groups, substituted and unsubstituted  
49 heterocycl groups, substituted and unsubstituted alkylaminoalkyl  
50 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
51 substituted and unsubstituted arylaminoalkyl groups, substituted and  
52 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
53 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
54 heterocyclalkyl groups, -C(=O)R<sup>25</sup> groups, substituted and  
55 unsubstituted aminoalkyl groups, substituted and unsubstituted  
56 heterocyclaminoalkyl groups, substituted and unsubstituted  
57 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
58 groups, substituted and unsubstituted aryloxyalkyl groups, and  
59 substituted and unsubstituted heterocycloxyalkyl groups;

60 R<sup>9</sup> and R<sup>14</sup> may be the same or different and are  
61 independently selected from the group consisting of H, -OH,  
62 substituted and unsubstituted alkoxy groups, substituted and  
63 unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted and unsubstituted  
64 alkylamino groups, substituted and unsubstituted arylamino groups,  
65 substituted and unsubstituted dialkylamino groups, substituted and

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66 unsubstituted diarylamino groups, substituted and unsubstituted  
67 (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
68 substituted and unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl  
69 groups, and -C(=O)-aryl groups;

70  $R^{10}$  is selected from the group consisting of substituted  
71 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
72 groups, substituted and unsubstituted heterocyclyl groups, substituted  
73 and unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl  
74 groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl  
75 groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)  
76 groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
77 -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
78 groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups,  
79 -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups,  
80 -C(=O)N(alkyl)(heterocyclyl) groups, and  
81 -C(=O)N(aryl)(heterocyclyl) groups;

82  $R^{11}$  is selected from the group consisting of H, -OH,  
83 alkoxy groups, aryloxy groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
84 groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups,  
85 substituted and unsubstituted alkyl groups, -NH(heterocyclyl) groups,  
86 -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, and  
87 substituted and unsubstituted aryl groups;

88  $R^{12}$  is selected from the group consisting of H,  
89 substituted and unsubstituted alkyl groups, substituted and  
90 unsubstituted aryl groups, and substituted and unsubstituted  
91 heterocyclyl groups;

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92 R<sup>13</sup> is selected from the group consisting of H,  
93 substituted and unsubstituted alkyl groups, substituted and  
94 unsubstituted aryl groups, substituted and unsubstituted heterocycl  
95 groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted and  
96 unsubstituted heterocyclalkyl groups, substituted and unsubstituted  
97 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
98 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
99 substituted and unsubstituted arylaminoalkyl groups, substituted and  
100 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
101 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
102 alkylamino groups, substituted and unsubstituted arylamino groups,  
103 substituted and unsubstituted dialkylamino groups, substituted and  
104 unsubstituted diarylamino groups, substituted and unsubstituted  
105 (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-  
106 aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -  
107 C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,  
108 -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
109 -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocycl groups,  
110 -C(=O)-O-heterocycl groups, -C(=O)NH(heterocycl) groups,  
111 -C(=O)-N(heterocycl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocycl)  
112 groups, -C(=O)-N(aryl)(heterocycl) groups, substituted and  
113 unsubstituted heterocyclaminoalkyl groups, substituted and  
114 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
115 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
116 groups, and substituted and unsubstituted heterocycloxyalkyl  
117 groups;

118 R<sup>15</sup> and R<sup>19</sup> may be the same or different and are  
119 independently selected from the group consisting of substituted and  
120 unsubstituted alkyl groups, substituted and unsubstituted aryl groups,

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121 substituted and unsubstituted heterocyclyl groups, substituted and  
122 unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl  
123 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)  
124 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -  
125 C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted  
126 and unsubstituted aminoalkyl groups, substituted and unsubstituted  
127 alkylaminoalkyl groups, substituted and unsubstituted  
128 dialkylaminoalkyl groups, substituted and unsubstituted  
129 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
130 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
131 substituted and unsubstituted heterocyclylaminoalkyl, substituted and  
132 unsubstituted diheterocyclylaminoalkyl, substituted and unsubstituted  
133 (heterocyclyl)(alkyl)aminoalkyl, substituted and unsubstituted  
134 (heterocyclyl)(aryl)aminoalkyl, substituted and unsubstituted  
135 alkoxyalkyl groups, substituted and unsubstituted hydroxyalkyl  
136 groups, substituted and unsubstituted aryloxyalkyl groups, and  
137 substituted and unsubstituted heterocycliloxyalkyl groups;

138 R<sup>16</sup> and R<sup>20</sup> may be the same or different and are  
139 independently selected from the group consisting of H, substituted  
140 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
141 groups, and substituted and unsubstituted heterocyclyl groups;

142 R<sup>17</sup> and R<sup>21</sup> may be the same or different and are  
143 independently selected from the group consisting of H, substituted  
144 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
145 groups, substituted and unsubstituted heterocyclyl groups, -C(=O)H,  
146 -C(=O)-alkyl groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -  
147 C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub>  
148 groups, -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups,

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149 -C(=O)O-alkyl groups, -C(=O)O-aryl groups, substituted and  
150 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted  
151 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
152 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
153 substituted and unsubstituted arylaminoalkyl groups, substituted and  
154 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
155 (alkyl)(aryl)aminoalkyl groups, -C(=O)-heterocyclyl groups,  
156 -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
157 -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocyclyl)  
158 groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and  
159 unsubstituted heterocyclylaminoalkyl groups, substituted and  
160 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
161 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
162 groups, and substituted and unsubstituted heterocyclyloxyalkyl  
163 groups;

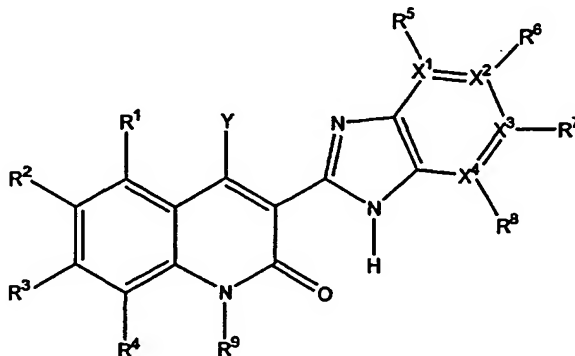
164  $R^{18}$ ,  $R^{23}$ ,  $R^{24}$ , and  $R^{25}$  may be the same or different and  
165 are independently selected from the group consisting of H, -NH<sub>2</sub>,  
166 -NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub>  
167 groups, -N(alkyl)(aryl) groups, -NH(heterocyclyl) groups,  
168 -N(heterocyclyl)(alkyl) groups, -N(heterocyclyl)(aryl) groups,  
169 -N(heterocyclyl)<sub>2</sub> groups, substituted and unsubstituted alkyl groups,  
170 substituted and unsubstituted aryl groups, -OH, substituted and  
171 unsubstituted alkoxy groups, substituted and unsubstituted aryloxy  
172 groups, substituted and unsubstituted heterocyclyl groups, -NHOH,  
173 -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl groups,  
174 -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, and -N(aryl)O-aryl  
175 groups; and

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176  $R^{22}$  is selected from the group consisting of substituted  
 177 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
 178 groups, and substituted and unsubstituted heterocyclyl groups,

179 and further wherein, at least one of  $R^1$ ,  $R^2$ ,  $R^3$ , or  $R^4$  is  
 180 an  $-OR^{15}$  group and  $R^{15}$  is selected from the group consisting of  
 181 substituted and unsubstituted heterocyclalkyl groups, substituted and  
 182 unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted  
 183 alkylaminoalkyl groups, substituted and unsubstituted aminoalkyl  
 184 groups, substituted and unsubstituted diarylaminoalkyl groups,  
 185 substituted and unsubstituted arylaminoalkyl groups, substituted and  
 186 unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and  
 187 unsubstituted heterocyclyl groups, substituted and unsubstituted  
 188 heterocyclalkylaminoalkyl groups, substituted and unsubstituted  
 189 diheterocyclalkylaminoalkyl groups, substituted and unsubstituted  
 190 (heterocyclyl)(alkyl)aminoalkyl groups, and substituted and  
 191 unsubstituted (heterocyclyl)(aryl)aminoalkyl groups.

1 23. The use of a compound of formula II, a tautomer of the  
 2 compound, a pharmaceutically acceptable salt of the compound, or a  
 3 pharmaceutically acceptable salt of the tautomer in treating cancer in conjunction  
 4 with an anti-cancer drug selected from 5-FU or CPT-11



II



**6** **wherein,**

Y is selected from the group consisting of H, -OH, -OR<sup>10</sup> groups, -SH, -SR<sup>11</sup> groups, -NR<sup>12</sup>R<sup>13</sup> groups, -CN, -C(=O)-R<sup>14</sup> groups, substituted and unsubstituted alkyl groups, substituted and unsubstituted alkenyl groups, substituted and unsubstituted alkynyl groups, substituted and unsubstituted aralkyl groups, substituted and unsubstituted heterocyclylalkyl groups, substituted and unsubstituted alkylaminoalkyl groups, substituted and unsubstituted dialkylaminoalkyl groups, substituted and unsubstituted arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted heterocyclylaminoalkyl groups, substituted and unsubstituted heterocyclyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl groups, and substituted and unsubstituted heterocyclyloxyalkyl groups;

23  $X^1$ ,  $X^2$ ,  $X^3$ , and  $X^4$  are selected from the group  
24 consisting of C and N, wherein at least one of  $X^1$ ,  $X^2$ ,  $X^3$ , or  $X^4$  is N;

**R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> may be the same or different and are independently selected from the group consisting of H, Cl, Br, F, I, -NO<sub>2</sub>, -CN, -OH, -OR<sup>15</sup> groups, -NR<sup>16</sup>R<sup>17</sup> groups, -C(=O)R<sup>18</sup> groups, -SH, -SR<sup>19</sup> groups, -S(=O)R<sup>20</sup> groups, S(=O)<sub>2</sub>R<sup>21</sup> groups, substituted and unsubstituted amidinyl groups, substituted and unsubstituted guanidinyl groups, substituted and unsubstituted primary, secondary, and tertiary alkyl groups, substituted and unsubstituted aryl groups, substituted and unsubstituted alkenyl**

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33 groups, substituted and unsubstituted alkynyl groups, substituted and  
34 unsubstituted heterocyclyl groups, substituted and unsubstituted  
35 alkylaminoalkyl groups, substituted and unsubstituted  
36 dialkylaminoalkyl groups, substituted and unsubstituted  
37 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
38 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
39 substituted and unsubstituted heterocyclalkyl groups, substituted and  
40 unsubstituted aminoalkyl groups, substituted and unsubstituted  
41 heterocyclaminoalkyl groups, substituted and unsubstituted  
42 hydroxyalkyl groups, substituted and unsubstituted alkoxyalkyl  
43 groups, substituted and unsubstituted aryloxyalkyl groups, and  
44 substituted and unsubstituted heterocycloxyalkyl groups; R<sup>5</sup> is  
45 absent or is H if X<sup>1</sup> is N; R<sup>6</sup> is absent or is H if X<sup>2</sup> is N; R<sup>7</sup> is absent  
46 or is H if X<sup>3</sup> is N; and R<sup>8</sup> is absent or is H if X<sup>4</sup> is N;

47 R<sup>9</sup> is selected from the group consisting of H, -OH,  
48 substituted and unsubstituted alkoxy groups, substituted and  
49 unsubstituted aryloxy groups, -NH<sub>2</sub>, substituted and unsubstituted  
50 alkylamino groups, substituted and unsubstituted arylamino groups,  
51 substituted and unsubstituted dialkylamino groups, substituted and  
52 unsubstituted diarylamino groups, substituted and unsubstituted  
53 (alkyl)(aryl)amino groups, substituted and unsubstituted alkyl groups,  
54 substituted and unsubstituted aryl groups, -C(=O)H, -C(=O)-alkyl  
55 groups, and -C(=O)-aryl groups;

56 R<sup>10</sup> is selected from the group consisting of substituted  
57 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
58 groups, substituted and unsubstituted heterocyclyl groups, substituted  
59 and unsubstituted heterocyclalkyl groups, -C(=O)H, -C(=O)-alkyl  
60 groups, -C(=O)-aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl

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61 groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl)  
62 groups, -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
63 -C(=O)N(alkyl)(aryl) groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
64 groups, -N(alkyl)<sub>2</sub> groups, -N(alkyl)(aryl) groups, -N(aryl)<sub>2</sub> groups,  
65 -C(=O)NH(heterocyclyl) groups, -C(=O)N(heterocyclyl)<sub>2</sub> groups,  
66 -C(=O)N(alkyl)(heterocyclyl) groups, and  
67 -C(=O)N(aryl)(heterocyclyl) groups;

68 R<sup>11</sup> and R<sup>19</sup> may be the same or different and are  
69 independently selected from the group consisting of substituted and  
70 unsubstituted alkyl groups, and substituted and unsubstituted aryl  
71 groups;

72 R<sup>12</sup> is selected from the group consisting of H,  
73 substituted and unsubstituted alkyl groups, substituted and  
74 unsubstituted aryl groups, and substituted and unsubstituted  
75 heterocyclyl groups;

76 R<sup>13</sup> is selected from the group consisting of H,  
77 substituted and unsubstituted alkyl groups, substituted and  
78 unsubstituted aryl groups, substituted and unsubstituted heterocyclyl  
79 groups, -OH, alkoxy groups, aryloxy groups, -NH<sub>2</sub>, substituted and  
80 unsubstituted heterocyclylalkyl groups, substituted and unsubstituted  
81 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
82 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
83 substituted and unsubstituted arylaminoalkyl groups, substituted and  
84 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
85 (alkyl)(aryl)aminoalkyl groups, substituted and unsubstituted  
86 alkylamino groups, substituted and unsubstituted arylamino groups,  
87 substituted and unsubstituted dialkylamino groups, substituted and

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88 unsubstituted diarylamino groups, substituted and unsubstituted  
89 (alkyl)(aryl)amino groups, -C(=O)H, -C(=O)-alkyl groups, -C(=O)-  
90 aryl groups, -C(=O)O-alkyl groups, -C(=O)O-aryl groups, -  
91 C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl) groups, -C(=O)NH(aryl) groups,  
92 -C(=O)N(alkyl)<sub>2</sub> groups, -C(=O)N(aryl)<sub>2</sub> groups,  
93 -C(=O)N(alkyl)(aryl) groups, -C(=O)-heterocyclyl groups,  
94 -C(=O)-O-heterocyclyl groups, -C(=O)NH(heterocyclyl) groups,  
95 -C(=O)-N(heterocyclyl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocyclyl)  
96 groups, -C(=O)-N(aryl)(heterocyclyl) groups, substituted and  
97 unsubstituted heterocyclylaminoalkyl groups, substituted and  
98 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
99 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
100 groups, and substituted and unsubstituted heterocyclioxyalkyl  
101 groups;

102 R<sup>14</sup> is selected from the group consisting of H, -OH,  
103 alkoxy groups, aryloxy groups, -NH<sub>2</sub>, -NH(alkyl) groups, -NH(aryl)  
104 groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub> groups, -N(alkyl)(aryl) groups,  
105 substituted and unsubstituted alkyl groups, substituted and  
106 unsubstituted aryl groups, -NH(heterocyclyl) groups,  
107 -N(heterocyclyl)<sub>2</sub> groups, -N(alkyl)(heterocyclyl) groups, and  
108 -N(aryl)(heterocyclyl) groups;

109 R<sup>12</sup> and R<sup>13</sup> may join together to form a 5 to 7  
110 membered saturated or unsaturated, substituted or unsubstituted N-  
111 containing ring;

112 R<sup>15</sup> is selected from the group consisting of substituted  
113 and unsubstituted alkyl groups, substituted and unsubstituted aryl  
114 groups, substituted and unsubstituted heterocyclyl groups, substituted

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115 and unsubstituted heterocyclylalkyl groups, -C(=O)H, -C(=O)-alkyl  
116 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)  
117 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups,  
118 -C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, substituted  
119 and unsubstituted aminoalkyl groups, substituted and unsubstituted  
120 alkylaminoalkyl groups, substituted and unsubstituted  
121 dialkylaminoalkyl groups, substituted and unsubstituted  
122 arylaminoalkyl groups, substituted and unsubstituted diarylaminoalkyl  
123 groups, substituted and unsubstituted (alkyl)(aryl)aminoalkyl groups,  
124 substituted and unsubstituted heterocyclylaminoalkyl groups,  
125 substituted and unsubstituted diheterocyclylaminoalkyl groups,  
126 substituted and unsubstituted (heterocyclyl)(alkyl)aminoalkyl groups,  
127 substituted and unsubstituted (heterocyclyl)(aryl)aminoalkyl groups,  
128 substituted and unsubstituted alkoxyalkyl groups, substituted and  
129 unsubstituted aryloxyalkyl groups, substituted and unsubstituted  
130 hydroxyalkyl groups, and substituted and unsubstituted  
131 heterocyclyloxyalkyl groups;

132 R<sup>16</sup> is selected from the group consisting of H,  
133 substituted and unsubstituted alkyl groups, substituted and  
134 unsubstituted aryl groups, and substituted and unsubstituted  
135 heterocyclyl groups;

136 R<sup>17</sup> is selected from the group consisting of H,  
137 substituted and unsubstituted alkyl groups, substituted and  
138 unsubstituted aryl groups, substituted and unsubstituted heterocyclyl  
139 groups, OH, substituted and unsubstituted alkoxy groups, substituted  
140 and unsubstituted aryloxy groups, -NH<sub>2</sub>, -C(=O)H, -C(=O)-alkyl  
141 groups, -C(=O)-aryl groups, -C(=O)NH<sub>2</sub>, -C(=O)NH(alkyl)  
142 groups, -C(=O)NH(aryl) groups, -C(=O)N(alkyl)<sub>2</sub> groups, -

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143 C(=O)N(aryl)<sub>2</sub> groups, -C(=O)N(alkyl)(aryl) groups, -C(=O)O-  
144 alkyl groups, -C(=O)O-aryl groups, substituted and unsubstituted  
145 aminoalkyl groups, substituted and unsubstituted alkylaminoalkyl  
146 groups, substituted and unsubstituted dialkylaminoalkyl groups,  
147 substituted and unsubstituted arylaminoalkyl groups, substituted and  
148 unsubstituted diarylaminoalkyl groups, substituted and unsubstituted  
149 (aryl)(alkyl)aminoalkyl groups, substituted and unsubstituted  
150 heterocyclalkyl groups, -C(=O)-heterocycl groups,  
151 -C(=O)-Oheterocycl groups, -C(=O)NH(heterocycl) groups,  
152 -C(=O)-N(heterocycl)<sub>2</sub> groups, -C(=O)-N(alkyl)(heterocycl)  
153 groups, -C(=O)-N(aryl)(heterocycl) groups, substituted and  
154 unsubstituted heterocyclaminoalkyl groups, substituted and  
155 unsubstituted hydroxyalkyl groups, substituted and unsubstituted  
156 alkoxyalkyl groups, substituted and unsubstituted aryloxyalkyl  
157 groups, and substituted and unsubstituted heterocycloxyalkyl  
158 groups;

159 R<sup>16</sup> and R<sup>17</sup> may join together to form a 5 to 7  
160 membered saturated or unsaturated, substituted or unsubstituted N-  
161 containing ring; and

162 R<sup>18</sup>, R<sup>20</sup>, and R<sup>21</sup> may be the same or different and are  
163 independently selected from the group consisting of H, -NH<sub>2</sub>, -  
164 NH(alkyl) groups, -NH(aryl) groups, -N(alkyl)<sub>2</sub> groups, -N(aryl)<sub>2</sub>  
165 groups, -N(alkyl)(aryl) groups, substituted and unsubstituted alkyl  
166 groups, substituted and unsubstituted aryl groups, -OH, substituted  
167 and unsubstituted alkoxy groups, substituted and unsubstituted  
168 aryloxy groups, substituted and unsubstituted heterocycl groups, -  
169 NHOH, -N(alkyl)OH groups, -N(aryl)OH groups, -N(alkyl)O-alkyl

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170 groups, -N(aryl)O-alkyl groups, -N(alkyl)O-aryl groups, and -  
171 N(aryl)O-aryl groups.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/10463

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07D 417/14, 413/14, 43/14; A61K 31/47

US CL : 546/157, 156, 155; 514/312; 544/60, 128, 363

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 546/157, 156, 155; 514/312; 544/60, 128, 363

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
CAS online

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/28993 A2 (MERCK & CO. INC) 26 April 2001 (26.04.2001), whole document.	11, 12, 23
P, X	US 2002/0107392 A1 (RENHOWE et al) 8 August 2002 (08.08.2002) whole document.	1-23
P, X	US 2003/0028018 A1 (RENHOWE et al) 6 February 2003 (06.02.2003) whole document.	1-23
P, X	US 2002/0103230 A1 (RENHOWE et al) 1 August 2002 (01.08.2002) whole document.	1-23



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See patent family annex.

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"O" document referring to an oral disclosure, use, exhibition or other means	"Z" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

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